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COMMUNICATIONS

THE VISUAL CELLS OF THE PLATYPUS *(Ornithorhyncus)*

BY

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In all vertebrate animals below the mammals it is the rule to find the cones present in both single and double forms. There are two varieties of the latter—" twin " and " double " cones. The members of the former are alike in every detail, whilst in the latter they differ in structure. The chief cone resembles its solitary neighbours and contains an oil-droplet, if they possess one; the accessory stains more delicately and contains no oil-droplet. In both types of double cones, although the elements appear to be fused in the greater part of their length, the end-plates and distal segments are free, and both units probably function independently. Because of the delicate structure of the accessory cone and of its intimate association with its partner, its observation is not always easy.

The accompanying drawings (with the exception of Fig. 5), were made with the *camera lucida* and a Zeiss 90X oil-immersion objective with 10X ocular from specimens prepared by the writer. To illustrate the gross retinal structure of a series of vertebrates, the drawings were made with the high power (Fig. 5). In this last diagram no attempt was made to represent the more delicate

details of structure, but merely to demonstrate similarities and differences between homologous layers in the retina of various members of the vertebrate family.

The twin-cones of the trout are very massive and the details of structure easily seen (Fig. 1). Both members are alike, and neither contains an oil-droplet. The finely granular nuclei are

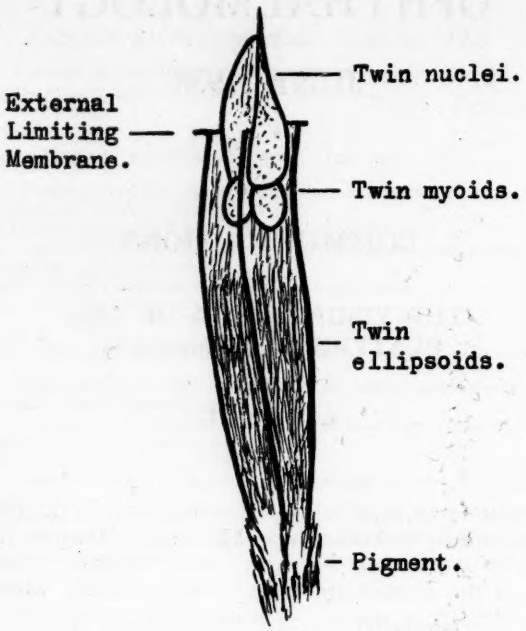


Figure I. Twin-cones of the trout.

bulging through the limitans. They do not seem to differ greatly from the rod-nuclei, except that the latter are confined within the external limiting membrane. The distal structure of the element is hidden within the densely-pigmented processes of the pigment epithelium. So dense is this that attempts at bleaching were only partially successful.

The double-cones of the pigeon are much smaller in structure (Fig. 2). The chief-member attains a deep purple with Mallory's connective-tissue stain, the ellipsoid staining more deeply than the

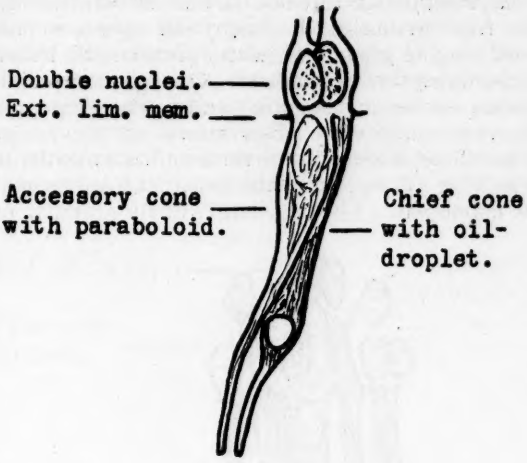


Figure 2. Double-cone of the pigeon.

myoid and swelling at its extremity to contain the oil-droplet. The distal portion is a long, thin cylinder, the details of which are hidden amongst the pigment epithelium. The granular nucleus is just within the limitans next to the nucleus of the accessory cone. Both resemble the rod-nuclei present in a single row above them. The accessory is in very close apposition to the chief-cone, so close that only after careful observation is it to be distinguished as a separate entity. Its outer segment is attached to the limitans by a broad base containing the paraboloid. Distally it rapidly narrows into a long, thin, cylindrical outer member. So close is its association with the chief-cone that, at first glance, the paraboloid often appears to be part of the structure of the latter. Its nucleus is just within the limitans next to that of the chief-cone.

Although Hoffman described the presence of oil-droplets in the cones of the marsupial[1], and Gunn in those of the monotreme[2], neither stated whether double cones were present. In view of the fact that both Greeff[3] and Rochon-Duvigneaud[4] state that the mammalian retina does not contain double-cones, the findings of the writer are of interest. Since reporting the presence of twin-cones with oil-droplets in the retina of the Australian native-cat (*Dasyurus viverrinus*)[5], examination of the ring-tail opossum

(*Pseudochirus laniginosus*) and the bushy-tail opossum (*Trichosurus vulpecula*), has revealed similar structures. Examination of the fresh retina of the bushy-tail opossum and of the kangaroo (*Macropus giganteus*) with apochromatic lenses, shows that the oil-droplets are colourless. Owing to the difficulty in obtaining material for investigation and in ensuring prompt and efficient fixation, satisfactory observations on the retina of the marsupial have been limited to the three animals mentioned above. The drawing (Fig. 4) represents the essential features of the twin-cone of the marsupial. The two, large, finely granular nuclei are

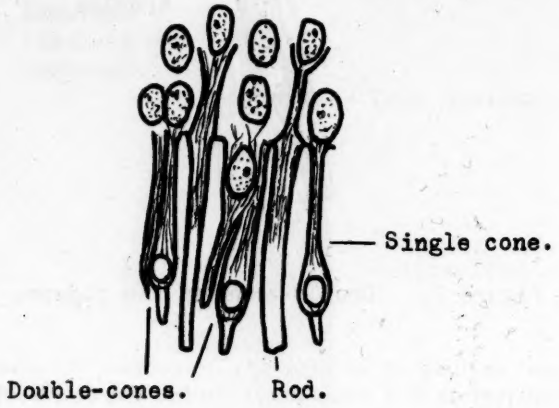


Figure 3. Visual cells of the platypus

seated side by side on the limitans, and present a marked contrast with the rod-nuclei which are present in overwhelming numbers and contain, in the case of the ring-tail opossum, one densely staining mass, and in the native-cat and bushy-tail, two or three. The purple (Mallory) slender myoid broadens out into the much more bulbous ellipsoid with the oil-droplet. The stumpy conical distal extremity can be seen to be in close contact with the pigment-epithelium in the pigment-free tapetal area. It stains a delicate shade of blue with a suggestion of transverse (or spiral) striation. Enclosing the ellipsoid is a delicate structure which the writer has referred to as the mantle.

Examination of the retina of the monotreme platypus (*Ornithorhyncus*) reveals a striking difference in the structure of its visual cells from those of the marsupial and higher mammal, and indeed, a close resemblance to that of the sauropsidae (Fig. 3). This is

not surprising as the monotreme (*Echidna* and *Ornithorhyncus* both) retains in its sclera the cartilage of the latter. In addition to single cones with oil-droplets, double cones are present, the chief member only containing the oil-droplet (Figs. 3 and 4). The visual cells are small and whilst the droplet-bearing cones and the rods stain vividly, the delicate accessory cones are made out with difficulty. In many instances the accessory nucleus is ectopic, that is it lies outside the limitans and renders the identification of the cell somewhat more easy. The nuclei are finely granular in

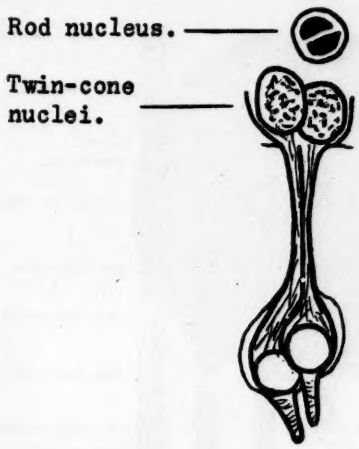
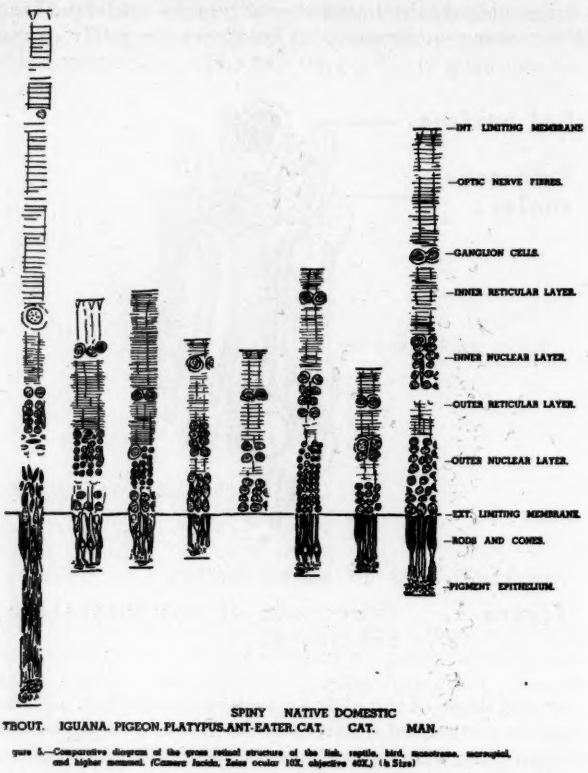


Figure 4. Twin-cones of the Australian native cat.

structure and those of the rods and cones are similar. In the chief-cone there is no marked differentiation in the staining of the myoid and ellipsoid, nor is the contrast in shape between the two very great. The distal extremity is a small, stumpy, blue-staining cone. The accessory stains much more delicately and uniformly from base to tip—a fine purple with a tinge of blue. With the nucleus in its usual position within the limitans, the outer segment often presents itself as little more than a delicate line. The rods are surprisingly massive and do not seem to outnumber the cones.

The comparative sparsity of the rods is remarkable in view of the commonly-held opinion that the animal is markedly nocturnal in its habits. When not disturbed, however, the fascinating little

creature hunts and feeds freely in brilliant sunlight. The relatively small eyes of both of the monotremes is further evidence that they are not strictly nocturnal, and present a marked contrast with the large globes of the nocturnal marsupials. The few massive rods of the former bear little resemblance to the multitudinous slender ones of the latter. There is a further difference in



gure 5.—Comparative diagram of the gross retinal structure of the fish, reptile, bird, monotreme, marsupial, and higher mammal. (Camera lucida, Zeiss ocular 10X, objective 40X.) (⅔ Size)

the structure of the nuclei of the visual cells. In the platypus the nuclei of both rod and cone are finely granular and indistinguishable as in the sauropsidae, whilst in the marsupial the very much more coarse distribution of the chromatin distinguishes the rod nucleus from that of the cone. In this the marsupial resembles the higher mammal.

The ratio between the number of nuclei in the outer and inner nuclear layers is unusual. Whilst the habits of the animal

apparently govern this ratio in each particular instance, in sauropsidae the inner nuclear layer usually outnumbers the two members of the outer nuclear layer, whilst in the higher mammal the reverse is the case (Fig. 5). The investigations of the writer tend to show that, in this respect, the marsupial resembles the higher mammal. Whilst the outer nuclear layer of the platypus is thicker than that of the bird and is nowhere less than three nuclei in thickness, nor more than four, the inner nuclear layer averages only four nuclei. This arrangement seems to bear a closer resemblance to that of the reptile and bird than to that of the higher mammal

FIG. 6.

and marsupial. The similarity in number of nuclei in the two layers as well as the thin layer of optic nerve fibres even in close proximity to the optic-disc, indicates a considerable degree of summation of visual impulses, a thesis which is not completely borne out by observation of the animal, which is very timid and darts away on the least movement of the observer.

Owing to the kindness of Mr. David Fleay of the Melbourne Zoological Gardens, a specimen of the spiny ant-eater (*Echidna*) was placed at the disposal of the writer. Unfortunately the animal had been dead for some hours before being placed in the fixative, and, on examining the sections, it was found that the outer layers of the rods and cones had disintegrated. The nuclei of the outer layer show a uniformly granular structure and are arranged in four layers at the most, whilst those of the inner layer are arranged in two or three.

The finding of double-cones in the retina of the monotreme and of twin-cones in that of the marsupial presents another interesting phenomenon to the student of comparative anatomy. A study of

the visual cells indicates that the marsupial and higher mammal are more nearly related to each other than to the monotreme. The latter resembles in many ways the sauropsidae. The absence of the pecten indicates a closer alliance with the reptile than the bird. As a probable reminder that the monotreme is, after all, a mammal, the intra-ocular musculature is unstriped.

The presence of ectopic nuclei calls for final comment. Heidenhain's iron haematoxylin proves that these structures are indeed nuclei and not paraboloids. Ectopic nuclei are found in the retina of man, the ape (*Cercopithecus*[6]), the domestic cow[7], and the lamprey[8]. Whilst Walls[9] is of the opinion that the position of the cone-nucleus is either permanently within or without the limitans in the higher vertebrates, the writer's sections of the platypus show occasional cones in which the nucleus appears to be streaming through the membrane as in the trout.

These investigations are being carried out in the Anatomy Department of the University of Melbourne under the direction of Professor Wood Jones, to whom the writer is indebted for his ever-ready help and valuable suggestions. He is also indebted to Sir James Barrett and Dr. Edward Ryan for supplying him with valuable material and for allowing him access to their libraries. The sections and photomicrograph were prepared with the assistance of Mr. H. Marriott.

REFERENCES

1. HOFFMAN, C. K. (1876-77).—"Zur Anatomie der Retina. II. Ueber den Bau der Retina bei den Beutelthieren." *Niederl. Arch. Zool.*, Bd. III, S. 195–8. Quoted by G. L. Walls.
2. GUNN, MARCUS (1884).—"On the eye of *ornithorhynchus paradoxus*." *Jl. Anat. and Physiol.*, Vol. XVII, pp. 400–5.
3. GREEFF, RICHARD (1900).—"Die mikroskopische Anatomie des Sehnerven und Netzhaut." *Graefe-Saemisch Handb. d. Augenheilk.*, 2 Aufl., Bd. V, Kap., S. 116.
4. ROCHON-DUVIGNEAUD, M. (1903).—"Anatomie de l'appareil nerveux sensoriel de la vision." *Encyclop. Franç. d'Ophtal.*, Vol. I, p. 618.
5. O'DAY, KEVIN (1936).—"A preliminary note on the presence of double cones and oil-droplets in the retina of marsupials." *Jl. of Anat.*, Vol. LXX, Part IV, p. 455.
6. GARTEN. 7. ZURN. 8. WALLS.—Quoted by Walls in
9. CULLER, A. M., and WALLS, G. L.—"Ectopic Cone Nuclei." *Arch. of Ophthal.*, Vol. III, p. 106, 1930.

THE OSMOTIC PRESSURE OF THE AQUEOUS HUMOUR IN EPIDEMIC DROPSY GLAUCOMA

BY

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Introduction

IN a previous paper by one of us (Kirwan, 1934) it was pointed out that epidemic dropsy is the only general disease at present known in which glaucoma forms an integral part and hence is the most important clinical lead we have ever had in the pathogenesis of glaucoma. With a view to the elucidation of the aetiology of primary glaucoma in general, this disease provides a vast field for research, for any advance to gain clearer views of an obscure intra-ocular condition is valuable.

Investigations into the causation of epidemic dropsy are still being carried out by various workers, but so far without success. Three main theories are at present held: (1) That it is produced by eating rice infected with certain bacteria, (2) That it is an infection which spreads by contact from person to person, (3) That it is due to some deleterious substance which is conveyed through mustard oil.

Different research workers have produced in the past experimental and epidemiological evidence in support of each of these theories. More recently the question of mustard oil being the incriminating factor has received particular attention. The presence of a toxic agent in the plasma of epidemic dropsy cases can now be considered to be established and this toxin produces a general dilatation of the capillaries and an increased permeability of their endothelial walls.

In the glaucoma associated with epidemic dropsy the whole uveal tract shows a marked dilatation of the capillaries without inflammatory changes. The aqueous shows a very marked increase of albumen, whilst the globulins remain the same. All the features theoretically necessary for an abnormal rise in the intra-ocular tension are found present and clinically increased tensions are actually observed.

One of the outstanding signs in this variety of primary glaucoma as pointed out in 1934 is that the anterior chamber, in spite of very high tensions, is seldom shallow and is nearly always

normal or even deeper than normal. This proves clinically that swelling of the vitreous body cannot be the cause of chronic primary glaucoma, and this fact has evidently been overlooked by Duke-Elder, Davson and Benham in their article on " the swelling pressures of normal and glaucomatous vitreous bodies " (September, 1936) in which they state that up to that date a decisive proof has been lacking.

In this research the osmotic pressures of the aqueous humour in normal eyes and in the glaucoma associated with epidemic dropsy were studied.

The chemical composition of the fluid from the anterior chamber of the eye has been very helpful in determining the origin and the nature of this fluid. Although some workers still hold that the aqueous humour originates as the secretion by the epithelium of the ciliary body of the eye the extensive researches of Duke-Elder (1937) and his co-workers have established that the composition of the aqueous humour is such that the concentrations of some of the ions present in it are related to those of the same ions in the plasma by a definite thermodynamic relation. Thus the concentrations in normality of sodium and chlorine ions in the two fluids have been shown by him to be related according to the equation :

$$\left[\dot{Na}\right]_{Aq} \times \left[Cl'\right]_{Aq} = \left[\dot{Na}\right]_{plasma} \times \left[Cl'\right]_{plasma}$$

where $\left[\dot{Na}\right]_{Aq}$ and $\left[Cl'\right]_{Aq}$ represent the concentrations of sodium and chlorine ions respectively in the aqueous humour, $\left[\dot{Na}\right]_{plasma}$ and $\left[Cl'\right]_{plasma}$ represent those in the blood plasma. The concentrations are in terms of normality.

This is obviously the condition characteristic of Donnan's membrane equilibrium, the existence of which is established in this case. These equilibrium considerations led Duke-Elder to the conclusion that the aqueous humour is a dialysate from the blood plasma and that capillary walls and not the capillary endothelium serve as dialysing membranes in such cases. Baurmann (1928) estimated the chemical constituents of an ultra-filtrate of serum and proved that the composition of the anterior chamber fluid is comparable to it. But more recently it has been pointed out by different workers that excepting the ions like $\dot{Na}$, $Cl'\dot{K}$, etc., there are a few other constituents whose concentrations in the aqueous humour do not bear out the existence of Donnan equilibrium as is observed in the cases of $\dot{Na}\,Cl'$, etc.

This, however, at first sight, presents great difficulties in the way of accepting the hypothesis of dialysation. But later researches by different workers have explained the anomalies in the concentration of some of the non-electrolytic substances as due to the metabolic activity within the anterior chamber (especially of the lens). But still there are other constituents, especially ions, whose concentrations continue to offer the same difficulty. Duke-Elder in 1936 has modified his older theory of simple dialysis. His present opinion on this point is that " aqueous humour is a dialysate from the blood plasma, showing the ionic distribution characteristic of such a system; superimposed on this simple system is the phenomenon of selective absorption which manifests itself in concentration gradients to certain molecules, but most probably not of Na^+, K^+ and Cl'." Thus he is of opinion that having dialysed from the intra-ocular capillaries and before reaching the chambers of the eye, the fluid passes through a physiological membrane, the properties of which maintain a concentration gradient to some molecules and a degree of unidirectional permeability to others (*cf.* Duke-Elder, 1937).

According to this hypothesis therefore any alteration in the permeability of either the capillary walls or the physiological membrane (mentioned above) or both, will bring about a change in the ionic concentrations in the aqueous humour. The escape of proteins into the aqueous humour will certainly increase the negatively charged micelles in it and as a result of the electrostatic forces the concentration of chlorine ions will tend to decrease and that of Na^+ ions to increase. A new equilibrium, again obeying the conditions of Donnan's membrane equilibrium but modified by changes in the membrane may be expected in such cases.

In epidemic dropsy the presence in the blood of a histamine-like base has been shown by Chopra and De (1937), which it is believed, brings about an increased permeability of capillaries, as well as a dilatation of these vessels. An increased amount of proteins has also been detected in the aqueous humour of the eye (*cf.* Kirwan, 1936). But it is not known to what extent the altered permeability affects the process of exudation of fluids and also the osmotic and hydrostatic equilibrium that are normally observed between plasma and this exudate. In the present paper an attempt has been made to ascertain whether in epidemic dropsy the same conditions obtain as in other cases of altered permeability of capillaries or whether the epidemic dropsy toxin brings about the adjustment of equilibrium between blood and aqueous humour in any other way independent of the membrane hypothesis. With this end in view the osmotic pressures of plasma and aqueous humour as well as their chlorine ion concentrations were determined and compared with those of normal subjects.

Experimental Portion

Specimens of 0·25 c.c. of aqueous humour from epidemic dropsy glaucomatous eyes were obtained from the Eye Infirmary, Medical College Hospitals, Calcutta. Blood sera of the same patients were also obtained. The fluid from the anterior chamber of the normal eyes was all obtained from aphakic eyes. The osmotic pressure was calculated from determinations of the relative lowering of vapour pressure by the thermo-electric method as suggested by Hill (1930) with slight modifications introduced by Baldes (1934). A galvanometer of the order of 10^{-11} was used and the scale was placed at a distance of about 10 metres from it, wherein the reflections were noted. The solutions to be tested were compared with 0·85 per cent. NaCl in every case after keeping both these fluids on the thermo-electric junctions at constant humidity for twenty minutes for the establishment of the equilibrium. It may be mentioned here that a 0·75 per cent. saline when balanced against a 0·85 per cent. saline always showed a deflection of 80 (+2) mm. on the scale. The osmotic pressures of plasma and aqueous humour have been calculated on the assumption that these fluids contain an equivalent amount of pure sodium chloride. Such an assumption can be justified in view of the minute quantities of other substances present in comparison with the preponderating amount of sodium chloride. The osmotic pressure of 0·85 per cent. saline was calculated to be 5,775 mm. of mercury from its data on the degree of electrolytic dissociation (*vide* Landolt-Bornstein Tabellen). The results have been tabulated below:—

TABLE I

(Normal Patients)

No.	Osmotic Pressure in mm. Hg		
	Serum	Aqueous humour	Difference
1	5873	5843	30
2	5881	5853	28
3	5881	5855	26
4	5937	5909	28
5	5901	5873	28
6	5894	5869	25
7	5850	5821	29
Average	5888	5860	28

TABLE II
(Glaucoma Patients)

No.	Osmotic Pressure in mm. Hg			Intra-ocular tension in mm. Hg
	Serum	Aqueous Humour	Difference	
1	5866	5857	9	36
2	5915	5901	14	40
3	5880	5859	21	36
4	5730	5715	15	50
5	5895	5874	21	36
6	5940	5918	22	38
7	5850	5831	19	40
8	5724	5704	20	40
9	5850	5838	12	56
10	5810	5795	15	57
11	5785	5771	14	70
Average	5840	5824	16	45

TABLE III
(Showing the average chlorine ion concentrations)

Nature of cases	Concentration of chlorine ions in	
	gms. per 100 c.c. of serum	gms. per 100 c.c. of aqueous humour
Normal - - -	0·3664 (1)	0·4435 (2)
Epidemic dropsy - -	0·5340	0·4298

(1) *Vide* Duke-Elder (1934).
(2) Findings of Mestrezat and Magitot (1921).

Discussion

Since the diffusible ions are unequally distributed a difference in osmotic pressure must exist between a dialysate and its parent fluid. A difference is obtained in fact, and Duke-Elder has shown that the osmotic pressure of the intra-ocular fluid corresponds exactly with that of a dialysate of the capillary blood in the normal state of the eye. In epidemic dropsy glaucoma the osmotic pressure difference is much less as compared to normal cases. The increase

of proteins in the aqueous humour and a consequent reshuffling of the diffusible ions make the aqueous humour more of a plasmoid type and the difference in the osmotic pressures is adjusted accordingly.

The osmotic pressure difference is always related to the intra-ocular pressure under equilibrium conditions by the relation that the blood pressure in capillary circulation exceeds the intra-ocular pressure. This amount is equal to the difference between the osmotic pressure of the two fluids. In other words, equilibrium is attained when the pressure of flow of fluid from the blood to the anterior chamber is exactly balanced by an opposite pressure from the intra-ocular fluid to the blood.

The diminution in the osmotic pressure difference between serum and aqueous humour (Table II) seems to be interesting in the light of these considerations. It evidently indicates that the difference between the capillary pressure and the intra-ocular pressure must also be as low. This, however, may be brought about in either of two ways:—Firstly, by a diminution of the first factor, viz., the pressure of the blood flow in the capillary, secondly by an increase in the intra-ocular tension. The dilatation of the blood tissues in the sub-epithelial connective tissues of the ciliary processes and the enormous dilatation of the capillaries of the choroid, as observed by Kirwan (1936), should certainly decrease the pressure of blood to a certain extent, but from observations on the blood pressure of epidemic dropsy patients it seems unlikely that it can account for the difference of pressure so low as that between the osmotic pressures of serum and aqueous humour. A low osmotic pressure difference between these two fluids, therefore, indicates that the intra-ocular pressure must rise considerably to bring about such a low value. Such abnormal rise of intra-ocular tension has been actually observed in all cases of epidemic dropsy glaucoma, and in fact a pressure about 50 mm. Hg is characteristic in these cases (Kirwan, 1936).

Regarding the origin of these increases of pressure it may be said that the alteration of the filtration angle of the eye does not appear to play an important rôle in this case, since Kirwan (1936) has observed that the channels of absorption in the eye, viz., the canal of Schlemm and tissues round it do not show any abnormalities either in cellularity or increased fibrosis. Thus it appears that the rise in the intra-ocular tension may not be the primary outcome of any decrease in the normal rate of drainage but rather of an accumulation due to increased inflow which the outlets cannot cope with.

The tension, therefore, owes its origin probably to a greater inflow of fluids than can be normally drained out. The albuminoid composition of the fluid in glaucoma cases obtained in epidemic

dropsy increases the osmotic pressure of the aqueous with a simultaneous diminution on the plasma side. The outflow of plasma into the aqueous is thus promoted and more and more fluids pass out from the blood till at last a back pressure is developed in the anterior chamber sufficient to prevent any further flow. The entire phenomenon thus seems to be due to the disappearance of proteins from the serum and their appearance in the aqueous due to an alteration of capillary permeability.

It will not be out of place here to discuss the effect of the change in permeability of capillaries. The escape of proteins raises the question : whether the change in permeability alters the nature of the filtration process, or, whether the same dialysation process governed by laws of Donnan's membrane equilibrium still operates as in normal subjects. The concentration of chlorine ions in blood serum and aqueous humour both in normal and epidemic dropsy subjects as given in Table III gives us a qualitative idea. According to Donnan's membrane hypothesis a higher chlorine ion concentration is expected under normal conditions in the aqueous humour than in the serum. That this is true is evident from Table III. If the membrane hypothesis holds in epidemic dropsy cases also there should be a small diminution of chlorine ion concentration in aqueous humour while that of serum should slightly increase. Such changes, however, do occur, as evident from Table III. It may, therefore, be inferred from these observations that change in the permeability of capillaries that occurs in epidemic dropsy does not alter the nature of the process of exudation of fluids from blood, but sets it at an altered state of equilibrium.

Summary and Conclusions

1. In epidemic dropsy glaucoma the difference between the osmotic pressure of blood serum and the aqueous humour is considerably reduced as a result of the appearance of proteins in the latter.

2. In consequence a reshuffling of ions takes place exactly in the same direction as predicted by the hypothesis of membrane equilibrium. The concentration of chlorine ions diminishes in the aqueous humour while an increase can be observed in the serum.

3. The evidence tends to support the view that in epidemic dropsy glaucoma the filtration of fluid into the anterior chamber takes place by the process of dialysation as usual, but that the equilibria concerned are at a level different from that of normal subjects, due probably to the altered permeability of the dialysing membrane.

We are indebted to Brevet-Colonel R. N. Chopra, C.I.E., K.H.P., I.M.S., Director of the Tropical School of Medicine,

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REFERENCES

BALDES, E. T. (1934)—*Journal Scientific Instruments*, Vol. XI, July.
BAURMANN. (1928)—*Ber. Ophthal. Ges.*, Heidelberg, Vol. XLVII, pp. 157-221.
CHOPRA, R. N., and DE. N. (1937)—*Indian Jl. Med. Research*, Vol. XXV, p. 101.
DUKE-ELDER, W. S., DAVSON and BENHAM. (1936)—*Brit. Jl. of Ophthal.*, Vol. XX, p. 520.
DUKE-ELDER, W. S. (1927)—*Biochem. Jl.*, Vol. XXI, p. 66.
——— (1934)—*Physiol. Rev.*, Vol. XIV.
——— (1936)—*Biochem. Jl.*, Vol. XXX, p. 773.
——— (1937)—*Brit. Jl. of Ophthal.*, Vol. XXI, p. 377.
HILL, A. V. (1930)—*Proc. Roy. Soc.*, Series A, Vol. CXXVII, p. 9.
KIRWAN, E.O'G. (1934)—*Arch. of Ophthal.*, Vol. XII, July.
——— (1936)—*Brit. Jl. of Ophthal.*, June, p. 321.
MESTREZAT and MAGITOT. (1921)—*Comp. rend. Soc. Biol.*, Vol. LXXXIV, p. 185.

STUDIES ON THE PATHOGENY OF TRACHOMA*

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DURING the course of studies pursued in this laboratory for the past six years on the aetiological relationships of trachoma, certain facts have been revealed which reflect the nature of the causative agent of this disease. It appears desirable at this time to bring together these facts in the manner of a recapitulation in order to construct a pattern of the pathogeny of trachoma.

In the work conducted thus far, it has been demonstrated, as others showed before us[1], that material derived from the conjunctiva of patients with trachoma, while completely innocuous for dogs, rabbits, hogs, guinea-pigs, rats, and mice, induces on the conjunctiva of monkeys an infection characterised essentially by folliculosis[2]. Preceded by an incubation period of several days to a month, the experimental disease frequently extends from the inoculated to the uninoculated eye and endures for a few weeks to many months, in some instances two and three years. The histological changes, although simulating those in trachoma, are

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not emphasised, because follicular reactions of the conjunctiva in general lack any features distinguishing the one from the other. Inoculation of trachomatous material in tissues other than the conjunctiva was found to be without effect. Tissues from different patients vary greatly in infective capacity, and despite the caution exercised in selecting only recent and clinically active disease, about half the tissues only are infectious. Conversely, individual animals (Macacus rhesus) exhibit a marked difference in susceptibility, approximately half the monkeys being resistant. It has not been possible to adapt the infection permanently in monkeys, since usually by the third serial passage the infectious agent is either lost or completely inactivated. Upon recovery, no resistance to infection or immunity to the experimental disease is demonstrable. Up to the present time, a hundred or more infected animals have been examined for the epithelial cell inclusions frequently observed in human beings, but neither scrape smears nor histological sections have revealed their presence.

Since the experimental disease lacks the two distinguishing signs of spontaneous trachoma (*i.e.*, cicatrization and pannus), experiments were performed[3] to indicate by virtue of its specificity the genuineness of the disease. Thus, human folliculosis, which in appearance may resemble the experimental disease, is not transmissible to monkeys; the formation of follicles is not stimulated by non-specific infection with a variety of bacteria, by irritation or by auto-inoculation of follicles occurring spontaneously in certain monkeys.

Experiments devised to elucidate the effect of faulty diet on the experimental disease[4] consisted of inoculating monkeys maintained on the diets deficient in vitamin A, or inadequate qualitatively and quantitatively in protein, or inadequate in protein and high in fat, or high in fat. The data indicate clearly that a state of malnutrition, as described with its resultant debilitation, does not predispose monkeys to trachoma; on the contrary, the animals appear to be less reactive than those maintained on an adequate diet.

Subsequently, in attempting to define the infectious agent of trachoma, an elaborate study was made of the bacteria cultivable from the disease. A number of workers have ascribed the causation of trachoma to different specific organisms[5], while other authors failed to find any characteristic bacteria[6]. It was found in this laboratory[7] that trachoma is not characterised by any particular flora, since the same bacteria may be isolated in similar frequency from other conditions of the eye, and to a less extent even from normal eyes. The variety of bacteria is extensive, and it remains unchanged in the different stages of the uncomplicated disease and is unrelated to the presence of inclusions. Inoculation

of the bacteria cultivated, either individually, pooled, or in conjunction with Berkefeld filtrates of infectious material, is without effect on monkeys, even though the tissues from which they are derived are of demonstrable specific infectivity.

The question of whether the infectious agent of trachoma is filterable has occupied the attention of previous workers. Some have succeeded[8] in transmitting trachoma with bacteriologically sterile fitrates, while others found such filtrates to be inactive[9]. In any case, however, the number of experiments conducted by the majority of the workers has been too small to include the different variables present in tissue infectivity and animal resistance. Filterability of the infectious agent was also studied in this laboratory by filtration through Berkefeld V filters. Of 14 experiments performed[10], the original material was infectious in 11. Filtrates of these tissues failed to infect monkeys of demonstrated susceptibility in 10 experiments, and in one the filtrate was as actively infectious as the material from which it was obtained.

Subsequently, the subject of filterability was restudied[11] to include variables in the process of filtration which might possibly interfere with the ready passage of the agent. Filtration of the infectious agent was attempted through Berkefeld V, collodion (average pore diameter about 0·6 μ), Seitz, and Kramer (plaster of Paris) filters. In seven experiments with material of demonstrated infectivity, filtration conducted in parallel with all four filters, filtrates were infectious only twice, and in each instance the agent traversed only the Berkefeld filter. In one of these two experiments, a collodion membrane (A.P.D. 0·93 μ), pervious to *B. prodigiosus*, was impervious to the trachomatous agent. In five other trials, collodion membranes alone were employed and their corresponding filtrates were deprived of the infectivity of the original materials. Thus, then, a total of 23 experiments have been undertaken during the two studies, and the infectious agent of trachoma was found to be filterable on three occasions. The evidence indicates, therefore, that bacteriologically sterile filtrates of human trachomatous tissues may retain their originally infective capacities. The infectious agent, however, is irregularly filterable and the difficulties of successful filtration may be attributable to variations both in the infectious tissues themselves and in the composition of the filter employed for the purpose.

The studies thus far reviewed suggest that the causative agent of trachoma is a virus. In order to obtain further evidence of its nature, adaptation was made of passing trachomatous tissues through rabbit testicle[12]. By such passage, the causative agent is liberated of extraneous bacteria and may be recovered in an active or infective condition (in 11 of 27 experiments). The absence during passage of any reaction, clinical or histological,

in the testicular tissue, the inability of the infectious agent to survive serial passage, and the maintenance of infectivity following recovery at approximately the original potency, all indicate that the causative agent does not multiply in the testicle but is merely preserved. Survivability in testicular tissue is not related with the presence of observable elementary or initial bodies in the original material nor with the formation of these structures in the testicle. Other experiments disclosed that successful passage of the agent may be accomplished occasionally by cerebral passage in rabbits, in which case no specific tissue reaction accompanies the successful passage.

The results already described in connection with testicular passage reveal the inability of the infectious agent of trachoma to multiply in the usual bacteriological media. A study was made, therefore, of cultivability in tissue cultures[13]. For this purpose, the technique devised by Maitland and Maitland of minced rabbit kidney[14], and as modified by Li and Rivers [15] of minced chick embryo, the developing chick egg (Woodruff and Goodpasture[16]; also Burnet and Galloway[17]), and various tissue fragments in plasma, were particularly utilised. In order to control both the methods and conditions of growth, similar experiments were carried out with the virus of St. Louis encephalitis, as already reported[18]. These methods of tissue cultivation were supplemented later by cultures made in plasma clots with human placental tissue extract and plasma from patients or normal individuals. In attempting to approximate very closely the conditions found in the eye, epithelial cells containing both the infectious agent (as demonstrated by inoculation of monkeys), and in some cases even inclusion bodies, were seeded by this method.

The technical difficulties accompanying the studies in tissue cultivation were numerous, the most consistent being the presence of adventitious bacteria in the original tissues. In the earlier seedings they were almost always present in the inocula, and they grew rapidly in culture, with the result that the growing cells were quickly destroyed or suppressed, thus defeating the purpose of the experiment. The use of several methods and chemicals, to inactivate selectively the bacteria only, was of no avail, since the infectious agent proved to be less resistant to the different substances. This obstacle was circumvented, however, by careful irrigation of the eye with salt solution, and then making multiple seedings of essentially epithelial scrapings collected in Tyrode's solution. While it was not possible to eliminate bacterial growth entirely in this way, bacteriologically sterile tissue cultures were frequently obtained. The seeded cultures were incubated both at 30° or 32°C. (to approximate the temperature of the conjunctiva)

and at 35° or 37°C., and incubation was carried out for three to seven days before transplants were made or before the cultures were nourished. Other cultures, under similar conditions, were made from infected eyes of monkeys and from testicular tissue carrying the infectious agent. In testing for infectivity, tissue cultures were inoculated in monkeys before and after transplanting and in every case the inoculum was derived from several cultures which had been pooled and triturated.

In summary, then, a total of 1,175 tissue cultures were made by cultivating and inoculating tissue from different animal species in 81 experiments, in 31 of which the original human material was infectious for monkeys. From 30 to 40 per cent. of the trachomatous materials employed in the different experiments on cultivation were found to contain epithelial cell inclusions. In none of the cultures, however, was it possible to demonstrate the presence of either constituent of the inclusion or the infectious agent of trachoma by inoculation of monkeys.

Cultivations attempted on a lesser scale in minced mouse kidney, in guinea-pig testicle, in the Brown-Pearce tumour of rabbits, in testicle and conjunctiva of monkeys, were all uniformly negative. In several instances, infectious material was inoculated in rabbit testicle simultaneously with a ground suspension of the rabbit tumour described by Brown and Pearce. Again the results indicate a failure of the infectious agent to grow. At other times, tissue cultivation was carried out anaerobically, as suggested by Dochez, Mills, and Kneeland[19], without, however, affecting the results already observed with other techniques. A few other experiments were attempted with cultivation of human placenta, but these were discontinued because of the difficulties encountered in growing this tissue.

The evidence is clear, then, that despite numerous attempts to cultivate the infectious agent of trachoma under a variety of conditions, in tissues from six different animal species, including man, and a cultivable rabbit tumour, it has not been possible to create *in vitro* the proper conditions for multiplication. While successful cultivation of the trachomatous agent in the fertile egg had been reported in a preliminary communication from India[20], a subsequent report[21] indicates that the original criterion of propagation was due to technical misinterpretations. More recently Poleff[22] has reported successful cultivation of the infectious agent by the Carrel technique and he identifies the agent as the inclusion body.

Experiments were subsequently conducted[23] to determine the susceptibility of the infectious agent to different chemical and physical agents. Recognising the danger of generalisation, since the variation both in infectivity of tissues and in susceptibility of

animals is great, it nevertheless seems fair to depict the characteristics to be described as typical of the infectious agent of trachoma. It is inactivated by heating at 45° to 50°C. for 15 minutes; it is rendered non-infectious by the action of ox-bile which causes lysis of epithelial cells and inclusions; it does not survive exposure to dilutions of 1·100,000 gentian violet, 0·25 per cent. phenol, 2 per cent. silver nitrate, 4 per cent. cocaine, and in about half the tissues tested even 2 per cent. cocaine, and tartar emetic in concentration of 1·1,000 is also destructive.

Preservation of the infectious agent of trachoma in glycerine has been reported by several workers, with a remarkable difference of opinion[24]. In most cases, however, the data are difficult of analysis, since little effort was made to determine either the original infectivity of the material or preservation under the same conditions without glycerine. In these experiments, the infectivity of the original suspensions was tested, and when they were found to be non-infectious, the data were discarded. The results of repeated experiments indicate that at ice box temperature glycerine does not maintain the infectious agent active any longer than preservation without glycerine. Ordinary preservation at this temperature varies, with different suspensions, from one or two days to a week or more. In general, however, tissues lose their activity within three or four days under these conditions.

The common clinical history of repeated infection in patients with trachoma was experienced in the experimental work when it was shown that monkeys acquire no active immunity to infection after recovery from the artificially induced disease. Nevertheless, an effort was made to determine whether human sera may act to prevent or diminish experimental infection. Conjunctival scrapings from patients, of verified infectivity, were mixed under different conditions of incubation with sera, whole blood, or plasma, derived in some experiments from the patients themselves, and in others from normal individuals. The results of these experiments indicate that blood from patients with trachoma contains no demonstrable substance capable of inactivating or neutralising the infectious agent, as measured by the development of experimental trachoma in monkeys.

Discussion

The accumulated studies on the aetiology of trachoma by numerous workers as well as ourselves no longer permit a reasonable rejection of the evidence that the disease is an infection in its own right without benefit of associated factors such as constitution, nutrition, co-related infection, etc. The exact nature of the infectious agent, however, has been in doubt for a long time,

but it is rapidly becoming more clearly visualised as a result of the more recent investigations. At the present time, the indications are that the agent is not a bacterium but a virus.

There are several reasons for considering the aetiological agent to be a virus. Most impressive, perhaps, is its inability to multiply on a number of bacteriological media, as well as in the more delicate environment of tissue culture. Occasionally by filtration, and more frequently by testicular passage, it may be liberated of any cultivable or visible forms and still retain its original infectivity. The exquisite tissue specialisation, species specificity, inclusion body formation, etc., are all added evidence of the viral nature of the infectious agent.

A recent development by Busacca[25], Cuenod[26], and Poleff[27] portrays the causative agent as a rickettsia, the most favourable evidence being the observation from Cuenod's laboratory[28] that inoculations of ground lice containing rickettsiae derived from trachoma may induce experimental trachoma in both monkey and man. By means of tissue culture, Poleff[22] identifies the rickettsial form as a component of the inclusion body first described by Halberstaedter and Prowazek and designated by them as the cause of trachoma. If, then, the rickettsial forms are indeed associated with the epithelial cell inclusion, the question of aetiology becomes less involved, as will be brought out presently.

While the inclusion body has been incriminated repeatedly in the past as the causative agent of trachoma, it remained for Thygeson, Proctor and Richards[29] to bring forward the weightiest argument in favour of this relationship. It will be recalled that in their hands a bacteriologically sterile filtrate of human trachomatous tissues was obtained with a collodion membrane impervious to *Bact. granulosis* and *H. influenzae,* that typical elementary bodies were found in the filtrate, and that the filtrate induced genuine trachoma in a human volunteer, as well as unmistakable inclusion bodies.

The question remains, then, whether the virus of trachoma is synonymous with the inclusion body or its component elements. This is, indeed a more fundamental question than trachoma, since it seeks the answer of a more general query perpetually raised by students of viruses regarding the identity or lack of identity of viruses and inclusions and without as yet a conclusive response.

It is beginning to appear, however, that viruses and inclusions may be, indeed, the same thing[30].

Consequently, by way of summary and conclusion, it may be said that the infectious agent of trachoma is characterised by low infectivity, occasional filterability, marked tissue specialisation, ineffectual immunogenic properties, slight propagative capacity, sensitivity to physical and chemical agents, and the

accompaniment of inclusion bodies. All these properties suggest the probability that the infectious agent is a virus. Whether the virus may be defined in turn as the inclusion body or its component elements remains to be proved, although the evidence available at the present time suggests this may be actually the case; whether again the inclusion body may be defined further as a rickettsia must also await upon future investigation. In the meantime, the three concepts of virus, inclusion body, and rickettsia are not so divergent as they appear at first glance; what differences each appears to have from the others are of the order less of fact and more of definition and classification.

BIBLIOGRAPHY

It would be impossible in a report of this kind to attempt more than a cursory reference to the extensive literature bearing on the various aspects of the aetiology of trachoma. A thorough review of the literature, with a more or less complete bibliography, will be found in a forthcoming monograph now in the press on the aetiology of trachoma, to be published by the Commonwealth Fund Division of Publications of New York.

1. HESS, C., and RÖMER, P.—*Arch. f. Augenheilk.*, Vol. LV, p. 1, 1906. HALBERSTÄDTER, L., and PROWAZEK, S.—*Deutsch. med. Wochenschr.*, Vol. XXXIII, p. 1285, 1907. HERFORD, E.—*Klin. Monats. f. Augenheilk.*, Vol. XLVII, p. 225, 1909. MORAX, W.—*Ann. d'ocul.*, Paris, Vol. CXLV, p. 414, 1911. HEYMANN, B.—*Klin. Monats. f. Augenheilk.*, Vol. XLIX, p. 417, 1911. NICOLLE, C., CUÉNOD, A., and BLAIZOT, L.—*Arch. Inst. Pasteur Tunis*, Vol. III, p. 185, 1911. ADDARIO, LA FERLA.—*Ann. d'ottal.*, Pavia, Vol. XIV, p. 278, 1912. OLITSKY, P. K., and TYLER, J. R.—*Science*, Vol. LXXI, p. 564, 1930; *Jl. Exp. Med.*, Vol. LIV, p. 31, 1931.
2. JULIANELLE, L A., and HARRISON, R. W.—*Amer. Jl. Ophthal.*, St. Louis, Vol. XVI, p. 867, 1933; Vol. XVII, p. 1035, 1934.
3. ——— *Amer. Jl. Ophthal.*, St. Louis, Vol. XVIII, p. 11, 1935.
4. HETLER, R. A., and JAMES, W. M.—*Amer. Jl. Ophthal.*, St. Louis, Vol. XVII, p. 1048, 1934.
5. SATTLER, H.—*Ber. Versamml. ophthal. Ges.*, Vol. XIII. p. 18, 1881. KOCH, R.—*Wien. klin. Wochenschr.*, Vol. XXXIII, p. 1550, 1883. MICHEL, J.—*Arch. f. Augenheilk.*, Vol. XVI, p. 348, 1885. MÜLLER, L.—*Wien. klin. Wochenschr.*, Vol. X, p. 920, 1897; *Arch. f. Augenheilk.*, Vol. XI, p. 13, 1900. RAEHLMAN, E.—*Beitr. z. Augenheilk.*, Vol. VII, p. 35, 1908. EDWARDS, P. T.—*Jl. Amer. Med. Assoc.*, Vol. XLIV, p. 965, 1910. WILLIAMS, A. W.—*Arch. of Ophthal.*, New York, Vol. XLII, p. 506, 1913. NOGUCHI, H.—*Jl. Exp. Med.*, Vol. XLVIII, suppl. 2, 1928. LUMBROSO, U.—*Arch. Inst. Pasteur Tunis*, Vol. XX, p. 253, 1931.
6. CAZALIS, C. A.—Trachome, Thèse de Montpellier, 1896. LAWSON, A.—*Roy. Lond. Ophthal. Hosp. Rep.*, Vol. XIV, p. 484, 1897. UHTHOFF. W.—*Zentrl. prakt. Augenheilk.*, Vol. XXII, p. 357, 1898. WAKIZAKA, K.—*Klin. Monats. f. Augenheilk.*, Vol. XLVII, p. 793, 1909. PACALIN, G.—*Arch. d'Ophtal.*, Paris, Vol. XLVII, p 690, 1930. SEIDLER, M., and STASINSKA, J —*Klin. Monats. f. Augenheilk.*, Vol. LXXXVI, p. 261, 1931. TABORISKY, J.—*Folia ophthal. orient.*, Vol. I, p. 34, 1932. THYGESON, P.—*Arch. Inst. Pasteur Tunis*, Vol. XXII, p. 157, 1933.
7. HARRISON, R. W., and JULIANELLE, L. A.—*Amer. Jl. Ophthal.*, St. Louis, Vol. XIX, p. 118, 1936.

8. BERTARELLI, E., and CECHETTO, E.—*Centr. Bakt., I. Abt., Orig.*, Vol. XLVII, p. 432, 1908. MARONGIU, L.—*Policlinico, sez. prat.*, Rome, Vol. XV, p. 805, 1908. NICOLLE, C., CUENOD, A., and BLAIZOT, L.—*Compt. rend. Acad.*, Vol. CLV, p. 214, 1912. OLITSKY, P. K., KNUTTI, R. E., and TYLER, J. R.—*Jl. Exp. Med.*, Vol. LIV, p. 557, 1931.
9. PFEIFFER, R., and KUHNT, H.—*Zeitschr. f. Augenheilk.*, Vol. XIII, p. 321, 1905. HESS, C., and RÖMER, P.—*Arch. f. Augenheilk.*, Vol. LV, p. 1, 1906. BAIARDI, P.—*Clin. ocul.*, Vol. VIII, p. 2719, 1907. FERMI, C., and REPETTO, R.—*Berl. klin. Wochenschr.*, Vol. XLIV, p. 1197, 1907. SZAFNICKI.—*Zentrl. ges. Ophthal.*, Vol. XXI, p. 45, 1929. TRAPESONTZEWA, C.—*Rev. internat. trachome*, Vol. VII, p. 65, 1930. LUMBROSO, U., and THYGESON, P.—*Arch. Inst. Pasteur Tunis*, Vol. XXII, p. 178, 1933. STEWART, F. H.—*Ann. Rep. Giza Mem. Ophthal. Lab.*, Vol. VIII, p. 142, 1933. CANDIAN, F. L.—*Atenca Parmense*, Vol V, p. 224, 1933. WRIGHT, R. E.—*Brit. Jl. Ophthal.*, Vol. XXI, p. 198, 1937.
10. JULIANELLE, L. A., and HARRISON, R. W.—*Amer. Jl. Ophthal.*, St. Louis, Vol. XVIII, p. 133, 1935,
11. ——— MORRIS, M. C., and HARRISON, R. W.—*Amer. Jl. Ophthal.*, 1937 (in press).
12. ——— and HARRISON, R. W.—*Trans. Amer. Acad. Ophthal. and Otol.*, p. 221, 1935; also *Amer. Jl. Ophthal.*, St. Louis, Vol. XX, p. 353, 1937.
13. HARRISON, R. W., and JULIANELLE, L. A.—*Amer. Jl. Ophthal.*, Vol. XX, p. 360, 1937.
14. MAITLAND, H. B., and MAITLAND, M. C.—*Lancet*, Vol. II, p. 596, 1928.
15. LI, C. P., and RIVERS, T. M.—*Jl. Exp. Med.*, Vol. LII, p. 465, 1930.
16. WOODRUFF, A. M., and GOODPASTURE, E. W.—*Amer. Jl. Path.*, Vol. VII, p. 209, 1931.
17. BURNET, F. M., and GALLOWAY, I. A.—*Brit. Jl. Exp. Path.*, Vol. XV, p. 105, 1934.
18. HARRISON, R. W., and MOORE, E.—*Proc. Soc. Exp. Biol. and Med.*, Vol. XXXV, p. 359, 1936.
19. DOCHEZ, A. R., MILLS, K. C., and KNEELAND, Y., Jr.—*Jl. Exp. Med.*, Vol. LXIII, p. 559, 1936.
20. PANDIT, C. G., WRIGHT, R. E., RAO, R. S., and SATYANATHAN.—*Indian Jl. Med. Res.*, Vol. XXIII, p. 475, 1935.
21. WRIGHT, R. E.—*Brit. Jl. Ophthal.*, Vol. XXI, 198, 1937.
22. POLEFF, L.—*Rev. internat. trachome*, Vol. XIII, p. 153, 1936; also *Arch. d'Ophtal.*, Paris, Vol. LIII, p. 882, 1936.
23. JULIANELLE, L. A., HARRISON, R. W., and MORRIS, M. C.—*Jl. Exp. Med.*, Vol. LXV, p. 735, 1937.
24. NICOLLE, C., CUENOD, A., and BLAIZOT, L.—*Arch. Inst. Pasteur Tunis*, Vols. III and IV, p. 157, 1913. BARONI, V., and MICHAIL, D.—*Rev. internat. trachome*, Vol. IX, p. 31, 1932. CANDIAN, F. L.—*Ann. ottal.*, Pavia, Vol. LXI, p. 890, 1933. STEWART, F. H.—*Ann. Rep. Giza Mem. Ophthal. Lab.*, Vol. VIII, p. 142, 1933; Vol. IX, p. 95, 1934. BUSACCA, A.—*Folia clin. biol.*, Vol. VII, p. 63, 1935.
25. BUSACCA, A.—*Folia clin. biol.*, Sao Paulo, Vol. V, p. 96, 1933: also *Arch. f. Ophthal.*, Leipsig, Vol. CXXXIII, p. 41, 1934.
26. CUENOD, A.—*Arch. d'Ophtal.*, Paris, Vol, LII, p. 145, 1935; also *Rev. internat. trachome*, Vol. XIII, p. 9, 1936.
27. POLEFF, L.—*Rev. internat. trachome*, Vol. XIII, p. 153, 1936.
28. CUENOD, A., and NATAF, R.—*Brit. Jl. Ophthal.*, Vol. XXI, p. 309. 1937.
29. THYGESON, P., PROCTOR, F. I., and RICHARDS, P.—*Amer. Jl. Ophthal.*, St. Louis, Vol. XVIII, p. 811, 1935; also *Arch. of Ophthal.*, New York, Vol. XIII, p. 1018, 1935.
30. BARNARD, J. E., and ELFORD, W. J —*Proc. Roy. Soc. Lond.*, Series B. Vol. CIX, p. 360, 1931-32. BEDSON, S. P., and BLAND, J. O. W.—*Brit. Jl. Exp. Path.*, Vol. XV, p. 243, 1934. LEDINGHAM, J. C. G.—*Lancet*, Vol. II, p. 525, 1931. PARKER, R. E., and RIVERS, T. M.—*Jl. Exp. Med.*, Vol. LXIV, p. 439, 1936. WOODRUFF, C. E., and GOODPASTURE, E. W.—*Amer. Jl. Path.*, Vol. V, p. 1, 1929; also Vol. VI, p. 712, 1930.

A MELANOSOME-DISPERSING SUBSTANCE IN THE BLOOD AND URINE OF PATIENTS WITH RETINITIS PIGMENTOSA

(Preliminary Communication)

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IN recent years there has been an increasing tendency to associate retinitis pigmentosa with pituitary dysfunction or diencephalic disturbance.

Such a relationship might be anticipated on embryological grounds from the common development of the optic vesicles and the diencephalon.

Clinical evidence gives further support to this connection. In the Laurence-Moon-Biedl syndrome retinitis pigmentosa is associated with obesity, hypogenitalism, polydactylism and mental deficiency, all probably indicating the manifestation of a specific hypophyso-diencephalic disturbance. At present the pathological evidence for a morbid process causing the syndrome is disappointing.

Although Stör in 1865 described a case which was probably an example of the above syndrome, and Fröhlich in 1901 described dystrophia adiposo-genitalis, none of Bell's three hundred odd references to the literature of retinitis pigmentosa, up to 1922, drew any special attention to a relationship between this condition and the pituitary body. In the last ten years an increasing number of papers have emphasised the association, in particular those of Zondek. He believes that abnormal hormonal influences from the pituitary body are probably produced by some interference in its co-ordination with the hypothalamus, resulting in the condition of retinitis pigmentosa. In collaboration with Koehler he gives evidence that cases showing pigmentary retinal degeneration without other abnormal clinical signs exhibit metabolic characteristics typical of his diencephalic syndrome (diencephalopathy).

Viallefont gives a brief summary of the evidence for the pituitary origin of retinitis pigmentosa, in which he believes, and describes the treatment of four cases with an extract of the whole pituitary gland; he was able to find four other accounts of similar treatment.

Recent Italian papers suggest an endocrine origin for retinitis pigmentosa, but none limits it to a diencephalo-hypophyseal disturbance. Most of the writers regard retinitis pigmentosa as being caused by hormonal action upon the local circulation, and suggest

that treatment with parasympathetic stimulants and vaso-dilators gives the best results.

Mecca observed five patients with retinitis pigmentosa for two years, and four of these showed abnormalities of the sella turcica and signs of neuro-endocrine disturbance. As a result of the study of these five and nine older cases he believes the main pathogenic factor is a spasm of the retinal vessels, due to endocrine action. Rinaldi holds much the same views, but thinks that independent functional or organic changes in the vessels of the retina or choroid may cause the condition.

Farina believes retinitis pigmentosa is probably due to a polyglandular endocrine disturbance. Schupfer, too, makes a critical survey of the literature. He holds the view that the diencephalo-hypophyseal theory alone cannot explain certain facts, such as the disturbances of smell and hearing and various congenital abnormalities of organs and tissues, not of ectodermal origin, which are found in many cases of retinitis pigmentosa. He concludes that inherited degenerative disturbances, especially of the mesodermal layer, play an important part in the pathogenesis of retinitis pigmentosa.

In contrast to the number of clinical observations there is little experimental evidence in support of an endocrine origin for retinitis pigmentosa. Some work is here described which suggests that a disorder of pituitary function is present in this condition.

In July, 1937, the writer undertook a classification of the various types of cutaneous pigmentation in this hospital, and samples of urine from selected cases were injected into frogs or toads, on the assumption that it might be possible to show the presence of a melanophore " expanding " substance. Later, working in conjunction with W. D. Brown, experiments were made with the urine from pregnant women. The method was next applied to two cases of the Laurence-Moon-Biedl syndrome in this hospital, and as both yielded positive results another six patients with retinitis pigmentosa were examined.

Method.—Jores and Will showed that " activation " of the melanosome—dispersing hormone of the pituitary body took place in alkaline extracts, and that if such solutions were boiled the potency was increased. Light is said to inactivate the hormone, particularly in acid solution. Therefore freshly passed urine was made just alkaline to litmus with tenth-normal caustic soda, immersed in a boiling bath for half an hour, and placed in a dark cupboard to cool.

The frogs were sorted according to their colour and size. Depending upon these factors the volume of urine given to each animal varied from 0·3 to 1 c.c., but was constant for all the frogs of any batch. The injections were made into the dorsal lymph sac.

One frog in each group received saline, and a second urine from a control. The control urines were selected at random by the nurses, and prepared in the same way as those of the patients with retinitis pigmentosa. Identification of the frogs was effected by coloured silks tied round their hind limbs. They were kept in daylight against a white background. After the method had been conclusively shown to succeed with intact animals, decerebrate frogs were used.

Results.—1. At first the experiments were performed without making any permanent record of the results. The following table shows the degree of colour change compared with the controls, 0 signifying a negative result, 1 an appreciable darkening, 2 a fairly deep colour, and 3 that the frog turned practically black. The letters in the vertical column represent the patients with retinitis pigmentosa whose urines were used.

INJECTIONS

	a	b	c	d	e	f	g
A	1	–	2	2	–	1	3
B	2	2	1	1	0	1	0
C	1	–	0	1	2	0	–
D	1	–	2	2	2	0	1
E	2	–	1	2	–	0	2
F	–	–	1	1	–	1	–
G	–	1	–	1	2	0	3
H	–	1	3	2	1	1	2

A and B are female cases of the Laurence-Moon-Biedl syndrome with well marked retinitis pigmentosa, C is a woman with all the signs of this syndrome except polydactylism. D is a female idiot with familial cerebellar hypoplasia and retinitis pigmentosa lately described by R. M. Stewart. E is a feeble-minded deaf-and-dumb girl with an extremely small sella turcica, as seen by X-ray examination; F a deaf, dumb and almost blind patient; G an idiot without obvious pituitary abnormality; and H an epileptic idiot. These last three cases are males.

It will be seen that the effects of injection were not constant, whereas on one occasion a frog would be turned very dark, on another the same patient's urine only produced a slight result, although there was usually a definite change compared with the controls. The results using large and very light-coloured frogs (injection " f " in the above table) were less impressive than in

slightly darker, smaller animals. Toads showed the melanosome dispersion easily, but the facility with which they changed colour of their own accord made them more difficult to use. The darkening took two to three hours to reach a maximum, and lasted a variable length of time from two up to twenty-four hours.

2. Photographs were taken of the frogs, the urines injected, and after two to three hours when the colour had changed they were photographed again. An example is shown in Plate 1.

PLATE 1. FIG. 1.

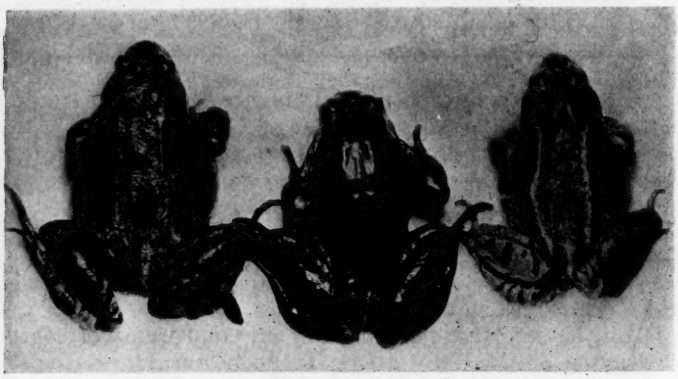


PLATE 1. FIG. 2.

The first photograph was taken before and the second two and a quarter hours after the injection of urine. The animal on the right was a control.

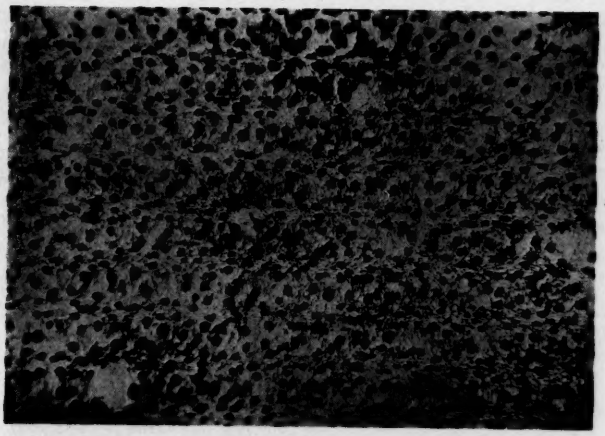


PLATE 2. FIG. 1.

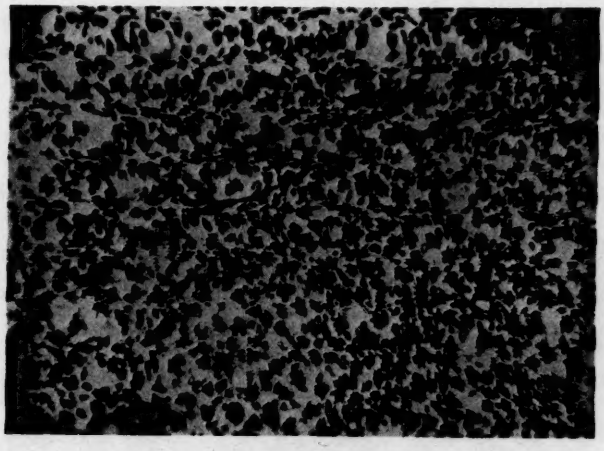


PLATE 2. FIG. 2.

Two low power photographs of skin from toads injected with urine, the first from a control, the second from a case of retinitis pigmentosa.

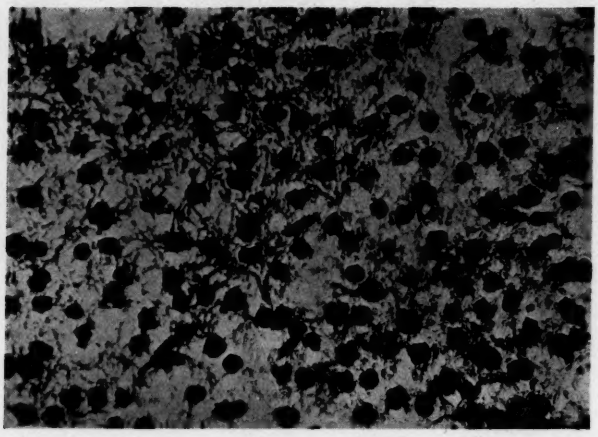


PLATE 2A. FIG. 1.

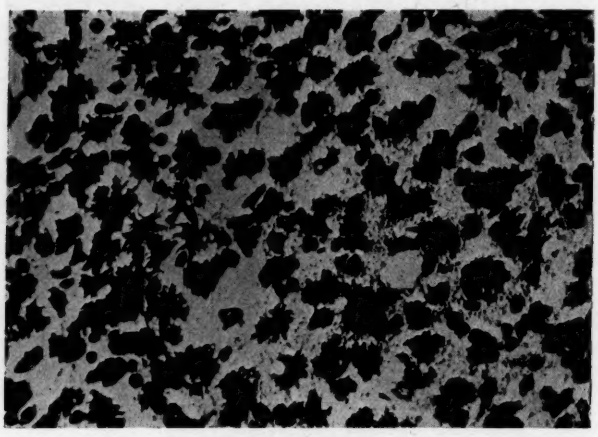


PLATE 2A. FIG. 2.

These are similar to Plate 2, but seen under high power.

Photographs by F. R. Hill.

3. Pairs of similar frogs were chosen, one injected with a control urine and the other with that from a case of retinitis pigmentosa. When melanosome dispersion had occurred they were killed, the skin removed, corresponding portions pinned to cork, and floated in either " frogs' " saline, glycerine, absolute alcohol, xylol, a solution of salicylic acid or formol-saline.

Some preparations were made by mounting directly, and some pieces were sectioned between liver to a thickness of 25μ. A photograph of a flat preparation is shown in Plate 2. The sections showed the melanophores as a series of discrete black masses in the control, whilst in the other there was an almost continuous line of pigment, the melanophores being less distinct.

4. Blood from these patients was freed from protein by introducing one volume into three of absolute alcohol. It was shaken, then allowed to stand over-night. The clear supernatant fluid was next removed, one volume of water was added, and the alcohol boiled off. The results of injection of 1 c.c. of this extract were variable like those of the urines, though usually constant for all the cases of retinitis pigmentosa. The skin, however, darkened more rapidly, often attaining its maximum depth of colour in one and a half hours, and the effect lasted longer than when urine was used.

5. Cerebro-spinal fluid from both the cisterna magna and the lumbar region was injected, but no melanophore expansion was seen, even when 2 c.c. were used.

6. Frogs were killed and from each, correspondingly situated pieces of skin were excised, pinned to cork, and floated in experimental and control urines respectively. After standing over-night the skin was removed from the urine, placed in absolute alcohol, and later cleared in xylol and mounted in balsam. A distinct difference in colour between the two specimens was now seen, and on microscopical examination a melanosome-dispersion was visible in the one but not in the other. The effect was sometimes seen microscopically in the one piece of skin even when injection of the same experimental urine into a frog had not produced an appreciable darkening.

Discussion.—It would appear from these observations that eight adult mental defectives with retinitis pigmentosa have a substance present in their blood and urine which is capable of dispersing the melanosomes of the frog. It could not be detected in either the cisternal or lumbar cerebro-spinal fluid by the method used.

From no other patients have samples of urine been found which give a similar result with the exception of certain cases of pregnancy, perhaps abnormal pigmentation of the skin, hyperthyroidism, and pituitary disease (Collin and Drouet, Jones).

Three of the eight have signs of pituitary dysfunction in addition to retinitis pigmentosa.

Collin and Drouet reported a melanosome-dispersing substance to be present in the urine on the day before or on the first day of menstruation. The above results do not apply to the urines collected on these days from the two females who menstruate.

It is known that a melanophore " expanding " hormone is found in the pituitary body but in no other tissue. The urine has not been shown to contain a substance capable of dispersing the melanosomes of the frog except in pathological conditions of the pituitary body, or at periods in which this gland is subjected to physiological stress. Thus from the little that is known concerning the substance found in the blood and urine of these cases of retinitis pigmentosa, it would appear probable that it is a hormone derived from the pituitary body.

Summary.—The blood and urine of eight adult mental defectives with retinitis pigmentosa contains a substance which will disperse the melanosomes of the frog.

A similar effect can be produced by the urine when there is pituitary abnormality or when the gland is subjected to physiological stress, but not in other conditions.

The evidence suggests that the substance in the blood and urine from these cases of retinitis pigmentosa is of pituitary origin.

I would like to thank Dr. R. M. Stewart, the Medical Superintendent, for suggesting the application of the method to these cases, for his help, and for allowing me to use the clinical material.

REFERENCES

BELL, J. (1922)—Treasury of Human Inheritance II, pt. I.
COLLIN, R., and DROUET, P. L. (1933)—*Bull. Acad. Med.*, Paris, Vol. CIX, p. 794.
*FARINA, F. (1936)—*Rass. Ital. d'Ottal.*, Vol. III, p. 566.
JONES, E. I. (1938)—*Lancet*, Vol. I p. 11.
JORES, A., and WILL, G. (1934)—*Z. ges. exp. Med.*, Vol. XCIV, p. 389.
*MECCA, M. (1936)—*Ann. di Ottal.*, Vol. CLXXII.
*——— (1936)—*Atti Cong. Soc. Ottal. Ital.*, p. 415.
*RINALDI, S. (1937)—*Rif. med.*, Vol. LIII, p. 371.
*SCHUPFER, F. (1937)—*Boll. d'ocul.*, Vol. XVI, p. 425.
STEWART, R. M. (1937)—*Sect. Neurol. R. Soc. Med.*, February 18.
STÖR, A. (1865).—*Klin. Monatsbl. f. Augenheilk.*, Vol. III. p. 23 (per J. Bell).
VAN DYKE, (1936)—Physiology and Pharmacology of the Pituitary Body. Chicago.
VIALLEFONT H. (1936)—*Ann. d'Ocul.*, Vol. CLXXIII, p. 33.
ZONDEK, H. (1935)—Diseases of the endocrine glands. London.
——— and KOEHLER, G. (1932)—*Deutsch. med. Wochenschr.*, Vol. LVIII, p. 2025.

*Abstracts of these papers appeared in *Zbl. f. d. ges. Ophthal.*. 1936-37.

A CASE OF PRIMARY BILATERAL ANOPHTHALMIA
(Clinical and Histological Report)

BY

ESMOND RECORDON *and* GWENVRON M. GRIFFITHS

CAMBRIDGE LONDON

THE subject of this report, a male child, was born on November 13, 1935, at March, Cambridgeshire.

No case of developmental abnormality had occurred in the family of either parent, and there was no consanguinity. Pregnancy and labour had been normal.

The mother, a primipara, aged 31 years, was one of a family of six. Her eldest brother is healthy; an elder brother and sister survived only a few hours; whilst two younger sisters are alive and well. The elder of these has produced one healthy child; the younger's first child died in infancy; a second survives and is normal. Her father died at the age of 62 years; her mother is alive and well. One maternal aunt died in a mental home.

The father, aged 37 years, had been married twice previously. There were no issue by his first wife, but one healthy child by the second. He was the eldest of a family of six, all of whom survive and are normal except the third who died in infancy. One of his brothers has a healthy child. His father is alive and well, but his mother had died two years previously.

A normal child has since been born.

Dr. J. A. Hislop, of March, invited one of us (E.R.) to see the infant when thirty hours old. It appeared to be normal in every respect apart from the entire absence of eyes. The birth weight was 7 lbs. 10 ozs. The eyelids were normal and the lacrymal puncta present. The palpebral apertures just admitted the tip of the little finger. Two smooth conjunctival sacs were explored but no vestige of a globe could be detected. The orbital cavities seemed to be smaller than normal.

The child progressed normally for a few days but later failed to put on weight, which on the tenth day was only 6¾ lbs. Breast feeding was only possible for the first week. It was admitted to Addenbrooke's Hospital, Cambridge, under the care of Dr. Leslie Cole, and gained weight steadily until shortly before its death (January 8, 1936) from bronchopneumonia. A post-mortem was performed and the brain and orbits removed for microscopic examination. The only abnormal post-mortem findings, apart from those relating to the visual apparatus, were a patent foramen ovale (which measured 2 by 3 centimetres), and bronchopneumonic changes in the lungs. The thymus was normal in size and the testicles had descended to the scrotum.

A detailed examination of half the brain and both orbits was made by one of us (G.M.G.) in the Pathological Laboratory, National Hospital, Queen Square, London :—

The brain appeared normal and well convoluted on its superior and lateral aspects. The base showed complete absence of the chiasma and optic tracts.

Serial sections in a frontal plane were made from the level of the olfactory trigone to the mid-pontine region and were stained for cells, myelin, neuroglia, and by silver impregnation for unmyelinated fibres. In these sections there was found no trace of optic tracts and nothing that could be identified as an external geniculate body. The hypothalamic region and infundibulum were intact with the nucleus paraventricularis and nuclei tuberis well marked. The supra-optic nucleus (Fig. 4), in the absence of an optic tract was lying flat, parallel to the meningeal surface and in one mass, instead of the normal two masses joined by a crescent of cells. The character of the cells and the vascularity appeared normal. The commissure of Meynert was well marked and well myelinated.

There was no abnormality of the basal ganglia, their fibre tracts, or of the internal capsule.

Between the mamillary bodies in the midline and projecting from the surface of the brain in a caudal direction was a teratoma 5 by 2 mm. (Fig. 5). It consisted of several small cysts or globules, lined with squamous epithelium, and in relation to these some digitating glandular structures. Some of these were possibly early hair follicles. One very small cyst was lined with goblet-cell (intestinal) epithelium. The cysts were lying in a mass of fibrous tissue with nerve cells and fibres (often encircling the cysts), and a mass of cartilage. The arrangement of the cysts and cavities suggested a rudimentary eye (especially in one area which looked like an eyelid), but the absence of pigment and the presence of gut proved its teratomatous nature.

In the midbrain no abnormality was found. The anterior colliculus showed the normal strata, though the cells were immature. (This was true of most parts of the brain owing to the age of the child.) The nuclei of the cranial nerves, third, fourth, fifth, sixth, seventh and eighth were well marked and well differentiated, and their nerves well myelinated, as was the posterior longitutinal bundle. The pineal gland was normal.

Sections were made of the posterior part of the brain, including the calcarine region and the horn of the ventricle. The area striata (Fig. 6) was rather small, but showed a well marked line of Gennari; the cells were mostly round and immature, but some were pyramidal in form. Silver impregnation showed the presence

of nerve fibres in this region, but there was very little myelin, and optic radiations could not be identified.

The sphenoid bone (Fig. 3) was well formed except that the optic canals were not patent. Very small ophthalmic arteries appeared to terminate at the bony wall. The pituitary fossa and gland appeared normal. The orbits were rather small and seemed macroscopically to be filled with fat.

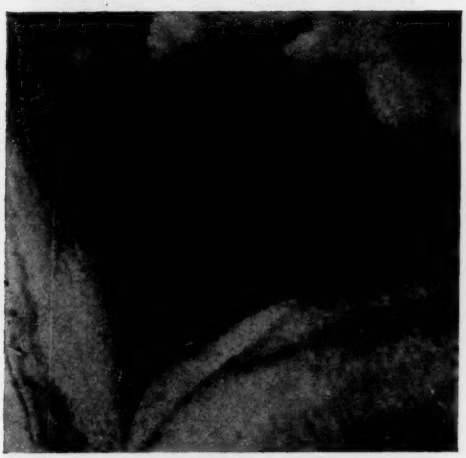


FIG. 1.

Anophthalmic baby, aged 5 weeks.

FIG. 2.

Medial aspect of brain. Showing absence of chiasma.

FIG. 3.

Sphenoid bone, showing ophthalmic arteries and flattening of bone over region of the optic foramina.

FIG. 4.

Nucleus supra-opticus, with the absence of optic tract.

Serial sections were made of the left orbit vertically and of the right orbit horizontally. In both orbits the six extrinsic muscles and their nerves were found, embedded in fat.

The oblique muscles were lying along the bony wall. In the left orbit (Fig. 7) the four recti were lying parallel to each other in the fatty mass, and at the anterior end were attached to a minute

FIG. 5.

Teratoma in region of mammillary body.

nodule of fibrous tissue, 163 by 85 by 240 microns. This nodule contained a quantity of pigment granules apparently lying free and not contained in any recognisable cell structure. The pigment was brownish and did not give an iron reaction. On the right side a similar but more minute mass of fibrous tissue was found (56 by 38 by 210 microns) (Fig. 8), but the muscles did not appear to be attached to it. In the nodules there was no trace of retinal neuro-epithelium nor any type of cell other than the fibrous tissue, and a little vascular tissue. Had the usual practice of examining

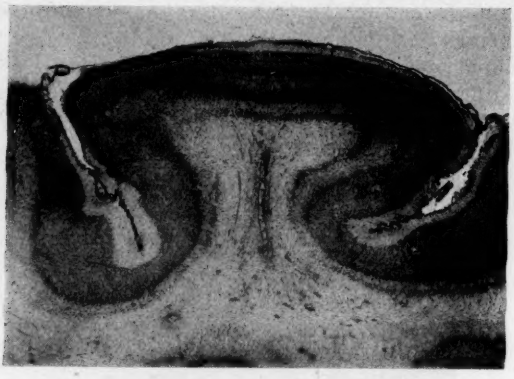


FIG. 6.

Cortex of calcarine region.

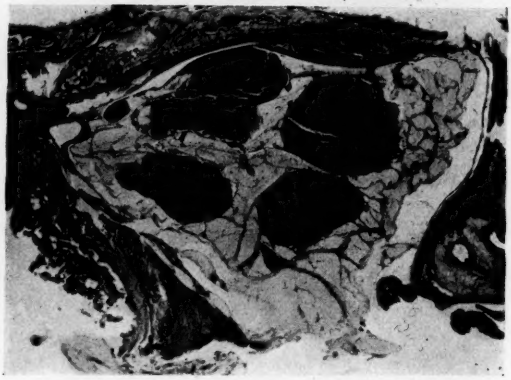


FIG. 7.

Vertical section of left orbit, showing the six extrinsic muscles.

every tenth section been adopted, either of these nodules might well have escaped detection.

This case, we maintain, is a proven one of bilateral primary anophthalmia, where there has been an absolute failure in the development of the optic vesicles, and is distinct from those cases of " degenerative " or " consecutive " anophthalmia in which the vesicles appear to have formed and subsequently to have atrophied.

(Cases belonging to the latter category have been described by Bietti, Cosmettatos, Haab, Redslob, also Souques and Bertrand.) Such a distinction cannot be made in the majority of the reported cases of this abnormality, since so few are accompanied by microscopical evidence. Cases in which orbital or palpebral cysts are described should not be termed " anophthalmia " of either type. Many reported cases are manifestly ones of extreme microphthalmia.

Perhaps the most conclusive case of primary anophthalmia that we have been able to discover in the literature (excluding the

FIG. 8.

Horizontal section of right orbit, showing fibrous nodule with pigment granules.

experimental and animal material) has been reported by Gallemaerts. The child described, a female, survived three months, and the abnormality was familial and hereditary. No trace of any rudimentary element could be discovered in the left orbit, but a heavily pigmented mass, 2·4 x 0·7 mm. was found in the right. The IVth and VIth cranial nerves were absent and there was irregularity in the position of exit of the IIIrd and Vth.

Van Duyse and Hanke have each reported a case accompanied by details of the orbital contents. Van Duyse found nodules of scleral and choroidal tissue measuring 1 x 5 mm. in the right orbit and 1 x 1 mm. in the left, and attached to some of the extrinsic ocular muscles. They appear to be similar to those found in our case, except that there were spaces and cells among the pigment and vessels, with stellate elements. One cannot feel convinced

that these nodules are entirely of mesodermal origin. In Hanke's case, the transverse section of the bulb rudiment resembles our case, but longitudinally there was a fibrous stalk, sheathed with pigment granules, and running back as far as the foramen.

Spiller, Finkelstein and Shaw Bolton report cases that are probably primary, but examination of the orbits was omitted. The histology of the brain has, however, been carefully worked out; Finkelstein paying particular attention to the external geniculate bodies which he found present but small, and Shaw Bolton to the calcarine cortex.

Because of the ease with which the optic outgrowth can be suppressed experimentally, Ida Mann believes that more cases should be conceded as " primary " than has been done in the past. The difficulty arises in proving that the pigment found in the orbit is entirely mesodermal in origin.

A nodule representing condensation of scleral tissue and containing minute particles of choroidal pigment is found in experimental primary anophthalmia, and there can be little doubt that the case here reported is one of that condition. The only other abnormalities discovered in this child, who died at the age of two months, were a brain teratoma and a patent foramen ovale. We suggest that the teratoma may have been responsible for the suppression of the optic vesicles.

We are indebted to Dr. J. A. Hislop for details of the family history; to Dr. Leslie Cole, who had the care of the child whilst in hospital; to Dr. J. F. Gaskell for the autopsy reports, and to Mr. K. Titterington for the photographs of the child and brain. We are also indebted to Dr. J. G. Greenfield for the microphotographs and helpful advice, and to Miss Ida Mann for her interest and suggestions.

REFERENCES

1. BIETTI.—*Ann. di Ottal.*, Vol. XXX, p. 319, 1901.
2. BOLTON, J. S.—*Phil. Trans. B.*, Vol. CXCIII, p. 161, 1900.
3. COSMETTATOS, G. F.—*Arch. d'Ophtal.*, Vol. XLVIII, p. 282, 1931.
4. VAN DUYSE.—*Arch. d'Ophtal.*. Vol. XIX, p. 412, 1899.
5. FINKELSTEIN, F.—*Schweiz. Arch. f. Neurol. Psych.*, Vol. XXXVII, p. 16, 1936.
6. GALLEMAERTS.—*Ann. d'Ocul.*, Vol. CLXI, p. 490, 1924.
7. HAAB, O.—*Beitrag. zur Ophthal. Festschr für Horner*, p. 131, 1881.
8. HANKE, V.—*Arch. f. Ophthal.*, Vol. LVII. p. 28, 1904.
9. MANN, I.—" Developmental Abnormalities of the Eye," p. 71, 1937. Cambridge University Press.
10. REDSLOB, E.—*Ann. d'Ocul.*, Vol. CLXIX, p. 133, 1932.
11. SOUQUES, A., and BERTRAND, I.—*Rev. Neurol.*, 38 (ii). p. 1, 1931.
12. SPILLER, W. G.—*Brain*, Vol. XXIV, p. 631, 1901.

A MODIFIED BRIGGS' RETRACTOR FOR DACRYOCYSTORHINOSTOMY

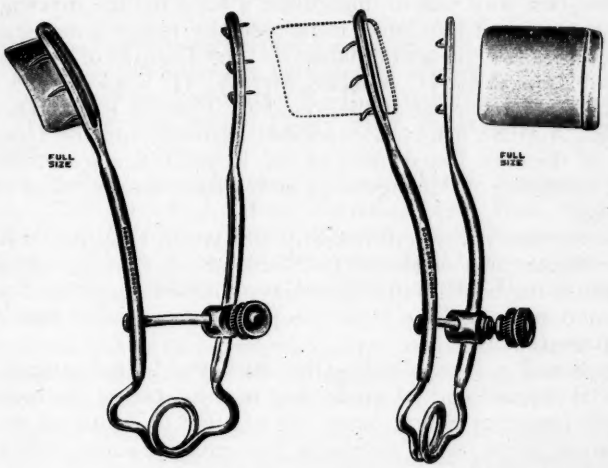
BY

H. B. STALLARD

LONDON

IN the operation of dacryocystorhinostomy good exposure and facilities for manipulation may be effected by the use of a retractor which I have termed a modified Briggs' lacrymal retractor.

The modifications consist in a broad blade-like termination of the shank on the temporal side. This shank is armed with three



blunt curved claws for insertion into the soft tissues and in addition has a slot 16 mm. long by $\frac{2}{3}$ mm. wide for the purpose of inserting a curved metal guard 16 mm. long by 18 mm. deep.

The guard is inserted through the slot at a stage in the operation when the sac has been dissected away from the lacrymal fossa and is drawn temporally, the guard being placed between the sac and the lacrymal fossa. By opening the retractor widely the lacrymal sac and orbital tissues are displaced to the temporal side and protected from injury during the removal of the oval window of bone from the lacrymal fossa. This instrument gives a good exposure, is neater and more exact than any hand retractor and also allows the assistant to have another hand free.

The instrument has been made for me by Down Brothers.

ANNOTATION

Research in the Prevention of Blindness

On April 20, 1938, the headquarters of the W. H. Ross Foundation for the Study of Prevention of Blindness was opened at 20, Lauriston Place, Edinburgh. The Foundation owes its initiation to the generosity of Mr. William H. Ross, who gave £40,000 for this purpose. Mr. Ross, in a speech which was read by Dr. Traquair, alluded to his own deterioration of sight, which, beginning in the year 1929, ended in total blindness in 1933.

Mr. Ross felt that he would like to be the means of saving his fellows from ever sharing the same fate, and eventually settled that the best way was to inaugurate a fund for the investigation into the causes of blindness, to be aided by research and study of the best means to prevent blindness. The Trustees of the Foundation are Dr. A. H. H. Sinclair, Mr. W. H. Fraser, W.S., and Mr. H. J. Ross, a son of the founder. Colonel R. M. Dickson, C.B.E., A.M.S., has been appointed Director, and the Honorary Staff of the Eye Department of the Royal Infirmary constitutes the Committee of Management under the Chairmanship of Dr. Sinclair.

The ceremony was performed by Mr. W. S. Douglas, Secretary to the Department of Health for Scotland, who, in a brief speech, alluded to the benefits that are likely to accrue from this Foundation, and promised the close co-operation and assistance of his department.

Dr. Sinclair, in explaining the work which had already been undertaken, said that he would only mention two of the investigations in progress. First, under the heading of industrial injuries, hypopyon ulcer of the cornea in coal miners, which represented 52 per cent. of all cases of corneal ulcer of this type treated at the Royal Infirmary. This investigation included an extensive examination of the bacteriology of the eyes of all classes of miners, some 800 having already been examined. The second line of research related to glaucoma.

The Foundation works in close co-operation with the medical faculty in Edinburgh, including the Royal Infirmary, and has the goodwill of ophthalmologists throughout Scotland. This was especially emphasized by Professor Ballantyne of Glasgow who pointed out that the prevention of blindness was a problem that could not be solved by individual effort but emphatically needed team work.

A description of the ceremony, accompanied by a leading article and an illustration appeared in " The Scotsman " of April 21,

and we should not omit to record our thanks to " The Scotsman " for most of the details given here. Mr. Ross will have the satisfaction of knowing how keenly his generosity is appreciated, not only in Scotland but throughout the empire and indeed the whole of the civilized world.

British Ophthalmology will wish God speed to the Foundation and the beneficent work which is undertaken.

THE COUNCIL OF BRITISH OPHTHALMOLOGISTS

Annual Report

The Council presents its report for the year 1937-38. At its first meeting in July the following were elected officers:—President: Sir John Parsons; Vice-Presidents: Mr. R. A. Greeves, Mr. F. A. Juler; Hon. Treasurer: Mr. A. H. Levy; Hon. Secretary: Mr. M. L. Hepburn.

The following were appointed to serve on the Executive Committee:—The President, Hon. Secretary and Hon. Treasurer (*ex-officiis*), with Messrs. Cardell, Greeves, Juler, Neame and Miss Ida Mann. Messrs. Juler and Neame were elected to represent the Council on the Ophthalmic Committee of the British Medical Association.

The Council has to record with much regret the death of Mr. William Lang who was one of the original members, but has been unable to take any active part in its work for many years.

During the year the Council has completed its investigations into the question of the visual standards required of candidates for L.C.C. Scholarships and Teacherships, and certain modifications of those laid down in 1924 have been made and approved by the Council. These new standards of vision have been accepted by the L.C.C. and are now being acted upon.

The Council continues to supervise the proceedings of the Orthoptic Board, a duty which it assumed two years ago. A register is kept of those qualified by examination to undertake Orthoptic training.

The expenses of the Council have been met out of the funds in the hands of the Hon. Treasurer, of which there is still a credit balance.

OPHTHALMOLOGICAL SOCIETY—ANNUAL CONGRESS

The Annual Congress of the Ophthalmological Society of the United Kingdom was held at the Royal Society of Medicine, London, on Thursday, Friday and Saturday, April 28, 29 and 30.

The President, Dr. Gordon Holmes, C.M.G., C.B.E., F.R.S., was in the Chair and gave an address of welcome to the visitors and members of the Society. The discussion on the differential diagnosis of the causes of exophthalmos was of considerable interest. The openers dealt with the ophthalmological, rhinological and general medical aspects of this disorder. It would be invidious to select any one or two papers for special praise among so many that were admirable scientific, pathological and clinical contributions to ophthalmology. Below is published an abstract of the papers.

DISCUSSION

"Differential Diagnosis of the Causes of Exophthalmos."

Openers:

Ophthalmic Aspects. By MR. R. FOSTER MOORE.

For the purposes of this discussion I have analysed in some detail 114 consecutive cases of proptosis, excluding cases of Graves' disease.

It is proposed first to consider the various means which are available for the differential diagnosis of the different causes of proptosis: a consideration of the general health of the patient; as to whether the proptosis is uniocular or binocular, the direction of the proptosis, whether it is reducible or pulsatile, the degree of immobility of the eye, the degree of chemosis, and palpation of the orbital cavity so far as this is possible.

Examination will include X-rays of the orbital cavity and surrounding sinuses, and a general examination of the patient for the investigation of any constitutional disease such as Graves' disease or leukaemia, which might be responsible for the condition, or the possibility of some primary growth which might have given rise to a metastatic deposit in the orbit.

Some consideration will be given to the cause of the proptosis of Graves' disease.

It is then proposed to consider in some detail the most important of the local conditions which cause an eye to be prominent: inflammatory conditions, traumatic causes, neoplasms, whether innocent or malignant, primary or metastatic.

Synopsis of the ear, nose and throat aspect of exophthalmos.
By MR. TERENCE CAWTHORNE.

Pathological conditions of the ear, nose and throat may produce exophthalmos either by causing an increase in the orbital contents or by reducing the size of the orbit. These mechanical effects may result from :—

1. Foreign matter being forced into the orbit.
2. Interference with the venous return from the orbit.
3. Extension of inflammation to the orbit.
4. Invasion of the orbit by new growth.

The history, rate of onset, whether the exophthalmos is unilateral or bilateral, the general condition of the patient, and the state of the ear, nose and throat, are the principal factors to be considered in arriving at a correct diagnosis of the cause.

Neurological and general medical causes of exophthalmos.
By DR. W. RUSSELL BRAIN.

1. *Diseases of bones of the skull.*

(i) Cranio-stenosis (oxycephaly). Variations in relation to the age of onset, symmetry and asymmetry of cranial changes and associated abnormalities. Spontaneous and voluntary dislocation of the eye.

(ii) Diabetic-exophthalmic dysostosis (Christian-Schuller-Hans disease. Xanthomatous erosion of orbits, pituitary and hypothalamus causing exophthalmos and diabetes insipidus.

2. *Increased intra-cranial pressure.*

(i) Hydrocephalus and tumours remote from orbit.

(ii) Tumours encroaching on orbit.

(*a*) Meningiomas. Sites in relation to orbit; intra-orbital extension of tumour. X-ray appearances.

(*b*) Osteoma of orbital roof : other tumours.

(*c*) Pituitary tumours and suprasellar cysts.

(iii) Intra-cranial aneurysm; sites in relation to orbit: exophthalmos before and after rupture: X-ray appearances.

3. *Vascular lesions.*

(i) Haemorrhage.

(*a*) Traumatic (*b*) due to hypertension (*c*) due to haemorrhagic diseases, *e.g.*, scurvy.

(ii) Venous obstruction.

(*a*) In cavernous sinus—due to (*a*) aneurysm (β) thrombosis.

(*b*) Due to intra-thoracic venous pressure:—associated with papilloedema.

4. *Endocrine diseases.*

(i) Exophthalmic goitre.

(ii) Exophthalmic ophthalmoplegia.

(iii) Pituitary adenoma. Recent evidence as to the rôle of the thyrotropic hormone of the pituitary in the production of exophthalmos.

Synopsis of paper on proptosis in children. By MR. J. H. DOGGART.

The principles of diagnosing the causes of proptosis are the same in children as in adults. Accessory methods of diagnosis are briefly considered.

In children proptosis occurs far more readily than in adults because:

(1) The eyeball itself is more distensible;

(2) The size of the orbit in relation to that of the eyeball is smaller than in adults.

The aetiology of proptosis is different in children. For instance, Graves' disease is almost entirely confined to adults; certain varieties of tumour are, on the other hand, unknown after childhood.

Lid retraction and exophthalmos in Graves' disease. By MR. E. E. POCHIN.

In cases of Graves' disease an appearance of exophthalmos may be produced by two different phenomena: first an actual proptosis and secondly a widening of the palpebral fissure by retraction of the upper lid, giving the illusion of exophthalmos.

The characteristics of this lid retraction were investigated in a group of cases of Graves' disease in which the retraction was unilateral and uncomplicated by any exophthalmos of the affected eye. This appearance is contrasted with that of the eye which is actually proptosed either owing to mechanical causes, or in such cases of Graves' disease as have exophthalmos, but give no evidence of lid retraction.

The following Members joined in the discussion:

MR. A. D. GRIFFITH briefly referred to arterio-venous aneurysm as a rare cause of proptosis.

MR. J. ELLISON.—Three cases of arterio-venous aneurysm of the internal carotid in the cavernous sinus are reported.

The mode of production of the condition is described and the effect on the circulation of the various methods of surgical treatment discussed.

MR. G. WILLOUGHBY CASHELL.—Description of case illustrating extreme proptosis following carcinoma of the antrum, which eventually involved the ethmoidal and sphenoidal sinuses and the base of the brain, illustrated with X-ray slides.

MR. A. F. MACCALLAN.—The following remarks are directed towards the inflammatory causes of exophthalmos only. The present speaker opened a discussion on this subject at this Society in 1928 (Vol. XLVIII, p. 1), when a classification of the causes of orbital inflammation was proposed. As a result of the study of recent cases and of recent literature a simpler classification is now offered.

The pathological changes in the orbit may be:—(1) Simple orbital oedema. (2) Orbital subperiosteal abscess. (3) Orbital cellulitis.

Orbital inflammations may originate from:—(1) Trauma. (2) The lacrymal apparatus. (3) Facial sepsis. (4) Dental sepsis. (5) The middle ear and mastoid cells. (6) The accessory nasal sinuses or nasopharyngeal inflammation. (7) Septicaemia or metastasis of septic material.

Remarks as to the differential diagnosis of these conditions are made.

"A case of glioma retinae, with special reference to the mode of spread." By MR. S. SPENCE MEIGHAN and MR. I. C. MICHAELSON.

A case of glioma retinae, with secondary deposits in the optic nerve, orbit, skull, lymph glands, and liver, is clinically and pathologically described.

A striking feature in the optic nerve spread was a jump in the tumour growth. Based on the facts in this case and of those reported in the literature, certain deductions are made regarding the mode of spread of such tumours.

Further operative procedure after removal of the globe for glioma retinae is discussed.

A brief histological description is given of the second eye in this case, which was also affected by glioma, and which was treated with success by radium.

"A case of meningocele of the orbit and the diagnosis from other tumours." By MR. M. H. WHITING.

A description is given of a case of posterior meningocele or encephalocele of the orbit, its development and the operative treatment; the diagnosis from other cystic conditions of the orbit is discussed.

"Remarks on ophthalmic gout." By MR. L. H. SAVIN.

Cases are described in which gout appeared to be the cause of ophthalmic disease. The literature of ophthalmic gout is briefly reviewed.

"A contribution to the pathology of angioid streaks." By MR. FRANK W. LAW.

A short review is given of the various theories which have been advanced in an endeavour to explain the phenomenon of angioid streaks. The clinical history and ophthalmoscopic appearances of a case which showed well marked angioid streaks are described, and from a study of the histological appearances conclusions are drawn which support the idea that angioid streaks are connected with folds in the retina.

"Abnormal retinal correspondence." By MISS E. E. CAS[illegible].

The term "retinal incongruity" was originally used in the 18th century to denote an abnormally placed, but normally functioning macula. The Nativistic school based their theories of space perception on Kant's philosophy and believed that corresponding points on the retina were anatomically fixed. The Empirists, headed by Helmholz believed in an acquired retinal correspondence and Pickford, von Graefe and others brought forward proofs of new found retinal relationships. Nagel believed that there was no such thing as corresponding points but said that binocular single vision depended upon the muscle sense and the overlapping of the visual fields. He said a squinting person had diplopia and false projection until his muscle sense told him the true position of his eyes and then he had true projection, no diplopia and binocular vision again. His theory does not explain physiological diplopia. Javal wished to avoid the term "retinal incongruity" and as von Graefe called the paradoxical diplopia which occurs after operations upon abnormal correspondence "false projection," he used this term for the condition of "abnormal correspondence," although he himself says it is a misnomer as these cases have "true projection" before operations. Little importance was paid to the condition of abnormal binocular vision in squinting persons from 1900 until the late "twenties."

False correspondence in the author's 500 cases occurred in a large proportion and some were seen in the course of development. Macular correspondence can be elicited in most cases of false correspondence, but if left late in life the patients relapse after operation and revert to their false correspondence. If operated upon early in life normal correspondence may quickly develop. Three groups occur.

1. *With false correspondence only:* occurring in amblyopic persons who do not improve on occlusion, and in alternators.

2. *True and false correspondence* where there are two places on the retina at some distance from each other (one being the macula) corresponding with the other macula. Squints over 10° and with moderate amblyopia. False correspondence moves nearer true on training.

3. *True and false correspondence, with fusion* with the macula of one eye over an area between the true and the false corresponding point in the other eye. The patients have a low angled often periodic squint, with either amblyopia rapidly improving on occlusion, or no amblyopia. Groups 1, 2 and 3 may change from one to the other according to conditions.

"Some aspects of the anatomy of the optic nerve-head." By MR. EUGENE WOLFF.

(*a*) The central connective tissue sheath, that is the connective tissue surrounding the central vessels does not come directly into relation with the vitreous, but is separated from it by glial tissue which Kuhnt called the central connective tissue meniscus. This is continuous with the internal limiting membrane which is thus absent over the central portion of the physiological cup.

(*b*) Neuroglia also separates the anterior portion of the scleral and the whole of the choroidal portions of the entrance canal of the optic nerve from the nerve fibres. This tissue is continued anteriorly beyond the pigment epithelium, where it forms the "intermediary tissue of Kuhnt," which is thought to be visible by the ophthalmoscope. This is discussed.

(*c*) The structure of the lamina cribrosa and the part it plays in the ophthalmoscopic appearance of the disc in the adult and new born baby are described.

(*d*) The origin of the capillary vessels which are responsible for the pink element in the colour of the disc is discussed.

"The history of contact lenses." By MISS IDA MANN.

The paper is a short resumé of the progress and evolution of ideas on the subject of contact lenses during the last hundred years, beginning with the theoretical discussion of them by Herschel in 1827. The subject will be dealt with under the headings of optical properties, tolerance, and therapeutic indications.

Optical properties. The two main types, focal and afocal contact glasses, will be described. In the former the resultant power depends on the radius of curvature of the glass and on the thickness of the "fluid lens" between it and the cornea. In the latter the contact glass is only separated from the cornea by a capillary layer of fluid and is itself a lens of the required power. Müller, Zeiss and Dallos lenses are discussed.

Tolerance. Whereas earlier workers in this field had concentrated almost entirely on obtaining the optimum optical result Heine emphasized the importance of a good scleral fit as the main factor in tolerance. The question of the superiority of blown glasses over ground glasses in this respect is due to their asymmetrical scleral portion, and recent work has been mainly directed to the scleral fitting. Heine, Czapody, Prister and Dallos have suggested various means of obtaining this.

Therapeutic indications. It is obvious that with improvements in fit and therefore in the possibility of good tolerance the range of suitable cases becomes wider. In the earlier stages only two indications were recognised, lagophthalmos and keratoconus. The list now extends to at least six classifications, i.e., (1) keratoconus and irregular astigmatism of all types, (2) high errors of refraction, especially high myopia and aphakia, (3) high degrees of anisometropia, (4) lagophthalmos, (5) occupational and cosmetic cases and (6) in certain investigations (fundus and slit-lamp examination and certain operations).

"Some observations on fluid interchange and its bearing on certain ophthalmological problems." By DR. J. DOUGLAS ROBERTSON.

If the aqueous humour is a dialysate, then the intra-ocular pressure should be maintained by the hydrostatic pressure in the capillaries minus the difference in osmotic pressure in plasma and aqueous. Evidence is brought forward that such a physical equilibrium does not always exist in the eye. The intra-ocular pressure has been studied in patients with very depleted plasma proteins and marked oedema, and in animals after alterations in the osmotic pressure of blood. The behaviour of the intra-ocular pressure suggests that the aqueous can no longer be regarded as a dialysate.

"Studies on the aqueous humour of normal and glaucomatous eyes." By MR. T. H. HODGSON.

The osmotic pressure of aqueous humour is higher than that of the corresponding blood serum. Pathological intra-ocular tension is not a simple function of either the osmotic or the chloride balance between the blood and the aqueous humour. Owing to the distribution of certain substances and to the osmotic relationship between the intra-ocular fluid and the blood it is impossible that the former is a simple dialysate.

"Detachment of the choroid." By MR. B. W. RYCROFT.

Choroidal detachment has been investigated in cases of glaucoma and cataract. Suggestions as to the aetiology are made. The prognosis and treatment are discussed.

"Vascular changes in the retina, optic nerve and kidney, a clinical and pathological study." By DR. A. J. BALLANTYNE, DR. I. C. MICHAELSON, and DR. J. F. HEGGIE.

A case of vascular hypertension, which came to post-mortem, and in which ophthalmoscopic examination of the retinal vessels had been made, is described. An attempt is made to correlate the histological vessel appearances with the changes found clinically. Parallel changes in vessels of comparable size in the kidney and brain are described.

The general pathological changes are those of essential hypertension. The heart which weighed 330 gms. was hypertrophied (small woman, stature 4 ft. 10 ins.). B.P. seven days before death 200 mm. Hg. The outstanding arterial lesions were found in the kidneys and brain. The former were not much reduced in weight, but showed areas of ischaemic atrophy in the cortex: the capsular aspects were finely granular. In the brain the arterial lesions were more advanced. The vessels of the circle of Willis were sclerosed and atheromatous, while the smaller vessels in the basal nuclei and medulla show elastic tissue proliferation with deposition of calcium salts and intimal thickening, and occasional thrombosis with resultant softenings.

"Associated lacrymal sac and partial mixed parotid tumour." By DR. J. PENDLETON WHITE, DR. I. C. MICHAELSON, and DR. J. F. HEGGIE.

Mixed tumours of the salivary gland type occasionally occur without these glands and recorded cases show them to have origin in several sites; palate, lip, tongue, etc.—"enclavements" at any point of fusion of the several embryonic processes which go to form the face. In the case here recorded a small tumour of this kind arose in the lacrymal sac of a man. It had been present for many years. Within six months of its removal a similar tumour was excised from the parotid gland on the same side. The occurrence of such tumours in the lacrymal sac is extremely rare.

"Observations on the treatment of epiphora." By MR. O. GAYER MORGAN.

The treatment of epiphora in cases of dacryocystitis with mucopurulent discharge from the sac is extremely difficult, and in many cases unsatisfactory.

Such a condition produces a disability out of all proportion to the extent of the pathological condition present, and to the afflicted patient, correct treatment means the difference between comfort, and extreme and continuous discomfort and danger.

Probing and other forms of local treatment seem to have only a very limited usefulness. Removal of the infected sac may obviate

some of the discomfort, but it is not really a satisfactory method of treatment in the majority of cases, and is unscientific in the cases in which the sac can be utilised in some other way.

A series of patients were treated by Toti's original method, and the results were not satisfactory. A further series treated by the method of Dupuy-Dutemps have given much better results, and although cases have to be chosen with care, this operation seems to be one which should be much more widely employed.

"A further communication on the aetiology and treatment of phlyctenular ophthalmia." By MR. A. SORSBY, MR. R. HAMBURGER, MISS MARGARET COVENEY, and MISS MARY E. NEVIN.

1. Analysis as to results of tuberculin tests and clinical evidence of tuberculosis in cases of phlyctenular ophthalmia admitted to White Oak Hospital, July, 1935—April, 1938.

Comparative data in blepharitis cases.

2. Comparative study of the significance of tonsillar sepsis in phlyctenular ophthalmia and in blepharitis.

3. The sedimentation rate of phlyctenulosis.

4. The tuberculosis contact rate in phlyctenulosis.

5. After history as to clinical tuberculosis in cases of phlyctenular ophthalmia admitted to White Oak Hospital, 1921-1931. Comparative study for cases of blepharitis.

6. Phlyctenular ophthalmia as a tuberculous allergy.

Demonstration :

"A living patient with fundus stained by green dye injection." MR. A. SORSBY.

"Evipan anaesthesia in ophthalmic surgery." By MR. T. K. LYLE.

The advantages of intravenous anaesthesia in ophthalmic surgery are shown in :—

A brief review of the cases at the Royal Westminster Ophthalmic Hospital for which evipan has been employed. (Evipan has been in use at the Royal Westminster Ophthalmic Hospital for the last four years).

A description of the technique of injection as employed at the Royal Westminster Ophthalmic Hospital.

Possible contra-indications and complications are mentioned.

"Paraldehyde analgesia." By DR. E. S. ROWBOTHAM.

A safe method of basal narcosis is described which renders the patient unconscious but not anaesthetic; local anaesthesia is used in addition. Paraldehyde in watery solution is given per rectum combined with omnopon where necessary.

Narcosis is followed by a period (which may be continued almost indefinitely) during which the patient remains asleep but can be roused for feeding.

Except in young children and old and debilitated subjects paraldehyde alone will not produce unconsciousness.

Cases may be grouped as follows:—

Group 1. ***Children under seven. Debilitated or severely toxic subjects.***—Chloretone suppository gr. x one hour before operation. Paraldehyde one drachm per stone weight three-quarters of an hour before operation per rectum.

(The solubility of paraldehyde in water is 1 in 10, so that each drachm of paraldehyde is dissolved in ten drachms of warm saline.)

Group 2. ***Normal adults and children over seven.***—One and a quarter hours before operation patient receives hypodermically omnopon gr. 1/30 for every stone weight; chloretone suppository gr. x followed in 15 minutes by paraldehyde one drachm per stone weight.

Group 3. ***Alcoholics, athletes, very nervous patients.***—These patients receive on the night before operation a bromide sedative. One and a quarter hours before operation omnopon gr. 1/30 per stone weight and hyoscine hydrobromide gr. 1/150. One hour before operation paraldehyde one drachm per stone weight.

To tide patient over post-operative period repeated small doses (one drachm to two drachms) of paraldehyde may be given.

"Cataract and other operations during deep sleep induced by paraldehyde and omnopon." By MR. BASIL GRAVES.

This is a safe hypnotic. The patients continue to sleep comfortably after the operation. It is suitable for cases of cataract, glaucoma, enucleation, excision of sac, trachoma expression and seemingly all eye operations for which it is considered that sleep is advantageous. Paraldehyde was first used therapeutically in 1882. Leech, of Manchester, in the Medical Chronicle, 1884-1885, suggested giving it per rectum. Morphia derivatives were in use long before that. Koller introduced cocaine as an eye anaesthetic in 1884. Some aspects of ophthalmic surgery are survivals of the pre-anaesthetic days and may advantageously be reviewed from this point of view.

Some problems of neuromyelitis optica. By DR. T. R. HILL.

The condition is contrasted with that of disseminated sclerosis, and an intermediate group of cases is described.

"Direct measurement of the axial length of the eye in the living subject by X-ray." MR. R. H. RUSHTON.

That the dark adapted eye is sensitive to X-rays had been noticed by early workers (Edison 1896, Röntgen 1897, Dorn 1898, Himstedt and Nagel 1901).

The phenomenon had not been further investigated until recent years. Gifford and Barth (*Arch. Ophthal.* 1934, p. 81) give an account of the early and recent work, together with some applications to ophthalmology.

The present paper describes the principle of a method of using the phenomenon for the accurate measurement of the axial length of the living eye. An instrument which embodies this principle has been used clinically and is described.

"A melanosome dispersing substance in the blood and urine in retinitis pigmentosa." By DR. E. C. DAX.

In the past ten years a number of writers have suggested that there is a relationship between retinitis pigmentosa and pituitary gland abnormality.

A substance which will disperse the melanosomes of the frog has been shewn to be present in the blood and urine of eleven cases of retinitis pigmentosa.

This substance has never been found in the urine except in pituitary disorders or when the gland has been subjected to physiological stress.

"Retinitis pigmentosa in rats." By MRS. D. R. CAMPBELL.

An account will be given of a hereditary retinal lesion in rats, which is primarily a degeneration of the rods and subsequently affects the pigment epithelium and other layers of the retina. The mode of inheritance and histological appearances bear a striking resemblance to retinitis pigmentosa and its mode of progress may be regarded as experimental evidence of the theory that this disease is primarily due to a degeneration of neuro-epithelium.

"Notes on dark adaptation and a simple instrument for its investigation." By MR. R. T. M. HAINES.

An apparatus designed to carry out tests for vitamin A deficiency by the dark adaptation test is described. Errors due to incomplete illumination of the retina and to subjective phenomena are eliminated or reduced. The intensity of illumination of the test object is controlled by the use of two polaroid discs one rotatable through a known angle. A number of dark adaptation curves are shown together with the affect of dosage with halibut liver oil on those subjects whose adaptation appeared to be abnormally poor.

Mr. M. L. HEPBURN joined in the discussion on the previous papers.

"The treatment of tobacco amblyopia by acetylcholine." By MR. P. MCG. MOFFATT.

A series of cases of tobacco amblyopia has been treated by acetylcholine, at the Royal Westminster Ophthalmic Hospital. The physiology and pharmacology of the choline compounds is discussed. Details of cases are given.

The Annual Dinner was held on Thursday, April 28, at the Langham Hotel. The President was in the Chair and proposed the health of the Society. He alluded to the importance of a close relationship between neurology and ophthalmology and referred to the activities of the Society in the past and of its association with famous neurologists and physicians.

Dr. Percival Hay proposed the toast of the Guests to which responses were made by Sir John Parsons and Major-General MacArthur. Mr. Leslie Paton proposed the toast of the President.

In connection with the Congress a trade exhibition of instruments and apparatus was held in the College of Nursing.

On Saturday afternoon facilities were afforded to some of the members to make a tour of the General Post Office. This was most interesting and instructive.

ABSTRACTS

I.—GLAUCOMA

(1) **Maziny (Cairo).—Statistical review of glaucoma in Egypt.** *Bull. Ophthal. Soc. of Egypt*, Vol. XXX, 1937.

(1) **Maziny** gives the percentage of glaucoma cases examined at the Egyptian Government Hospitals during the last twenty years. He shows that with the enormously increased number of new patients, which in 1935 amounted to more than a million, the percentage of glaucoma has diminished from 3·25 per cent. in 1919 to 0·73 per cent. He points out that this is due to the increased attendance of patients with less serious ocular conditions, and is not due to any defects in the recording of cases of glaucoma.

In the discussion *Zaki* stated that the highest incidence of glaucoma at the Minia Hospital was 4·5 per cent. in 1923, while in 1935, it was 1·2 per cent. It is remarkable that in the year 1934 he saw 392 glaucomatous patients at this hospital.

A. F. MACCALLAN.

(2) **El Kattan (Egypt).—Glaucoma.** *Bull. Ophthal. Soc. of Egypt*, Vol. XXX, 1937.

(2) **El Kattan** reports an interesting case of glaucoma in a young lady of 26 years of age. She had an acute congestive attack in both eyes with a tension of about 80. The fact that it was bilateral and in so young a patient was remarkable. A history of nasal trouble was obtained, and sinusitis of both maxillary antra and of the ethmoidal cells was found. A few days after these had been drained the intra-ocular tension dropped to 17.

The pathological condition was a double Tenonitis secondary to the sinus inflammation, with subsequent pressure on the vortex veins, and the production of a severe congestive type of glaucoma.

A. F. MACCALLAN.

(3) **Ibrahim, F. G. (Egypt).—Syphilis among glaucomatous cases.** *Bull. Ophthal. Soc. of Egypt*, Vol. XXX, p. 40, 1937.

(3) A provocative dose of neosalvarsan was given before operation to 220 patients upon whom glaucoma operations were to be performed, and to 142 patients who were to be operated on for cataract. It was found that 17·2 per cent. of the glaucomatous patients, and 13·3 per cent. of the cataract patients were Wassermann positive. Most of the patients were operated on successfully, after having been given about 2·5 grammes of neosalvarsan intravenously, and several intramuscular injections of 1 per cent. perchloride of mercury solution.

A. F. MACCALLAN.

(4) **Maghraby, A. (Egypt).—Glaucoma capsularis.** *Bull. Ophthal. Soc. of Egypt*, Vol. XXX, p. 42, 1937.

(4) **Maghraby** states that in 1936 he detected 19 cases of exfoliation of the lens capsule among 18,000 new cases examined at Zagazig Ophthalmic Hospital. Of these 19 cases, glaucoma developed in 16.

He refers to an interesting paper by Sohby on the same subject published in Vol. XX, p. 3, of the same Journal.

A. F. MACCALLAN.

(5) **Nicolato (Pavia).—The changes in the optic nerve in primary glaucoma. (Considerazioni sulle alterazioni del nervo ottico nel glaucoma primario).** *Rass. Ital. d'Ottal.*, September-October, 1937.

(5) **Nicolato** had the opportunity of examining the eye of a patient suffering from primary glaucoma who died as a result of broncho-pneumonia. He finds marked changes in the part of the

nerve in front of the lamina cribrosa; the fibres in the middle of the nerve are broken up irregularly and have lost their capacity of receiving stains. The peripheral fibres retain their normal characters and pass over the scleral edge unaltered to the retina. The lamina cribrosa is unchanged in position and appearance. The supporting glial tissue breaks up after the loss of the nerve fibres, and the cup in the papilla contains only small detritus.

The author compares these changes with those which may be found in the region of the iridic angle in chronic glaucoma, and believes them to be due to the altered condition of nutrition, and changes in the intra-ocular fluids. The chief cause cannot be the raised intra-ocular pressure since the middle fibres are those first affected; further, the disappearance of the glial tissue marks a difference between this state and other forms of atrophy.

HAROLD GRIMSDALE.

II.—MISCELLANEOUS

(1) **Carleton, E. H. and Madigan, L. F. (Hanover, N.H.).—Relationships between aniseikonia and ametropia.** *Arch. of Ophthal.*, Vol. XVIII, p. 237.

(1) The good clinical results obtained by the correction of the aniseikonia in a large number of patients lead **Carleton** and **Madigan** to stress the importance of examination for this anomaly in all cases with functional disturbances of the eyes, including those that are not relieved by correction of their refractive errors or motor abnormalities.

Cases of emmetropia and isometropia, in which an appreciable amount of aniseikonia was corrected, show that the latter may exist independently of ametropia.

The presence of anisometropia suggests the possibility of concomitant aniseikonia, but the coefficient of correlation of 0·6 between the differences in the sizes of the retinal images and differences in refractive power indicates that, although a correction for ametropia may be a partial cause of aniseikonia in the general run of patients, there is in many cases no relation between the two—in certain cases of anisometropia there may be no aniseikonia, while in others the correction of the ametropia may actually tend to reduce rather than increase the basic aniseikonia.

It is concluded that on the basis of the ametropia no arbitrary deductions as to the probable amount of aniseikonia in any specific case can be made.

THOS. SNOWBALL.

BOOK NOTICES

Oftalmologia dei Paesi Caldi. (Tropical Ophthalmology). By Professor VITTORIO RUATA. Pp. XI and 362, with 4 Coloured Plates and 91 Illustrations in the Text. Milan: Hoepli. Price, 45 Lire.

In this pleasantly written and well printed book, Professor Ruata has given to the ophthalmic surgeon practising in the tropics, a most useful guide. It shows not only the nature of the diseases which are special to hot countries, but also the modifications of the every day diseases common to all climates which are met with in the tropics, for, as Professor Ruata points out, it is these latter which will make up the greater number of the conditions requiring diagnosis and treatment. The book is made up of nine chapters; in the first, those conditions are described which are due to local atmospheric conditions; the glare of many desert lands has an effect on the functions of the eye; both acuity and extent of the visual field may be diminished. There is sometimes a ring scotoma, sometimes a concentric contraction; both of these would be a source of grave danger in aviation. These symptoms are often accompanied by occipital headache, and appear gradually after the subject has been living for some time in the hot region; proper protective glasses are capable of preventing the disturbance of function. The second, third and fourth chapters deal with the diseases caused by animal and vegetable parasites, and the ways in which they gain entrance to the eyes. Animal parasites in most cases attack the eye in their larval form; the identification of the species is not easy, owing to the small size and similarity of appearance. It must in most cases be done by an entomologist. The vegetable parasites, bacteria, are common to all countries but in some cases, as for instance the gonococcus, their mode of life differs; in Egypt this germ is a common inhabitant of the conjunctiva and is carried from eye to eye.

There are three chapters on diseases of the conjunctiva and cornea, one being devoted to trachoma; due attention is paid to the importance of prophylaxis. In the chapter on the cornea, many other conditions are touched upon, including glaucoma and cataract. Then follows a chapter on the ocular manifestations in general diseases, and this is probably the section most interesting to those in tropical countries, since many of the diseases are seldom, if ever, seen in temperate regions. A short chapter on surgical methods completes the book. It is a pleasure to read this book and to find the author conversant with the English literature of ophthalmology. There are few misprints except in the spelling of names other than

Italian; this is always a difficulty when dealing with names of others than of one's own race. The legend to Fig. 67 should be "sarcoma dell'orbita" and not "tracoma dell'orbita" and two Figs. 66 and 69 are more easily recognised if turned upside down. But apart from these minor errors the whole deserves all praise.

A Textbook of Ophthalmology. By SANFORD R. GIFFORD, M.A., M.D., F.A.C.S., Professor of Ophthalmology, Northwestern University Medical School, Chicago; Attending Ophthalmologist, Passavant Memorial, Cook County, Wesley Memorial and Evanston Hospitals. Volume of 492 pages, 249 Illustrations, 12mo. London and Philadelphia: W. B. Saunders Co., Ltd. Price, 18/- net.

The opening chapters of this book on "Methods of Examination" are commendably short and their theoretical aspect not over stressed; this is surely of advantage in the consideration of that branch of the subject which can only be satisfactorily learnt in contact with the patient.

There follow chapters in which each structure of the eye, the orbit and extra-ocular muscles are dealt with in routine manner. In addition to the more common diseases a number of considerable rarity, some of which scarcely merit inclusion in a book of this size, are reviewed. The diseases of the optic nerve and higher visual pathways are particularly clearly and concisely stated, and the chapter on injuries to the eye is detailed and informative.

The coloured plates and diagrams are excellent throughout the book, but many of the photographic reproductions lack the definition essential in portraying clinical conditions.

The scope of this book is comprehensive and its outlook modern; at the same time the medical student, for whom the author states this book is primarily written, may well be excused some dismay when faced with these 460 pages, so crowded with information, on a subject which can only occupy a minor place in his curriculum.

International Ko Test Type.

Tatsuji Inouye's Ko type is so-called on account of the smybol ⌋ employed in this type which bears some resemblance to the Japanese phonetic character "Ko." The charts are used at 5 metres distance and may be placed horizontally, vertically or upside down to decrease the chance of memorizing by the patient. The Ko type size 5/5 and Landolt's ring type 5/5 can be distinguished from the same distance. The sign $\frac{<}{>}\ \frac{m}{F}$ indicates whether the capacity to count fingers at the given number of metres is equal or unequal to the corresponding Ko type number. Five types are supplied (1) Large size

white paper, complete types, vision 0·02—2·0. (2) Large size white paper, vision 0·02—0·15. (3) Large size black paper, vision 0·02—0·15. (4) Medium size white paper, vision 0·1—2·0; with astigmatic chart. (5) Medium size, white paper for wall hanging and test type box, vision 0·1—2·0.

The white type on black background is better for the examination of patients suffering from photophobia.

The children's chart consists of simple line drawings in black on a white background. The chart is intended for use at 5 metres but the author suggests that the child be taught the names of the objects at close range and then stand at 1 metre from the chart and read it. The visual acuity is arrived at after consulting a chart plotted to give the corresponding 5 metre visual acuity at ranges of ½ metre to 4 metres. The principle of the Ko symbol ⊐ is similar to the E test used in this country and to Landolt's ring test.

The charts are clear and simple in construction. Detailed information is given in the *Klin. Monatsbl. f. Augenheilk.*, Bd. XCV, s. 750, 1935.

Proceedings of the All-India Ophthalmological Society. Vol. V, Session. 1936.

The Proceedings of the All-India Ophthalmological Society, Vol. V, 1936, contains the original papers read before the Fifth Conference of the Society held at Lahore on December 18, 19, 21, 1936.

The report of the Society shows a steady increase in its membership which has now reached 154, and it also comments on the increased number of the scientific contributions and their quality.

The papers are mainly on matters of clinical and practical interest, among which is "A symposium on diabetes and eye affections"; two papers reporting cases of corneal grafting; eight on cataract; seven on glaucoma; two on retinal detachment and the others on subjects of current interest, in all forty-three papers. There are four coloured plates illustrating cases of keratoplasty. There are a number of other good monochrome illustrations and an index. The Presidential address contained an account of certain aspects of ophthalmic work and their relation to Public Health in India under the present social and economic conditions. The President dealt with such matters as dietetic deficiency, ophthalmia neonatorum, smallpox, ophthalmic inspection and care of schoolchildren and the prevention of industrial injuries.

We hope to publish at a later date abstracts of some of the scientific papers.

Transactions of the Ophthalmological Society of the United Kingdom. Vol. LVII, Part 2, Session 1937. London: J. and A. Churchill, Ltd. Pp. 235. Illustrated. 1938.

Part 2 of volume LVII of the *Transactions of the Ophthalmological Society of the United Kingdom* has just been published. It contains the scientific papers read at the Oxford Ophthalmological Congress in 1937 and the Midland Ophthalmological Society 1936-37.

Among many papers of scientific and clinical value the discussion on the problem of myopia; the Doyne Memorial Lecture by the late Dr. David James Wood (Cape Town)—Night blindness in eye disease—suggestions and speculations; Sir Walter Langdon-Brown's paper on hormones and vitamins in ophthalmology; Professor Imre's description of plastic operations of the eyelids, and Dr. Dallos' paper on the individual fitting of contact glasses are outstanding. There is also a coloured plate illustrating ochronosis.

The index of parts 1 and 2 of volume LXII is at the end of part 2.

CORRESPONDENCE

VALUE OF ORTHOPTIC TRAINING

To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.

DEAR SIRS,—I have carefully studied with interest Mr. Law's article in last month's number of the ***British Journal of Ophthalmology.***

It is refreshing to read at the outset that "it is high time that an impartial investigation was conducted in order to discover whether the immense amount of time and trouble now being devoted to orthoptics is bearing the fruits of success which one is entitled to expect from so highly organised and extensively practised branch of ophthalmology," but as one continues to read the article it becomes obvious that impartiality has not been strictly observed.

Figures quoting results of treatment can be converted into percentages so as to give a false impression, and one cannot help feeling that this is the case under consideration.

Mr. Law states in referring to Abnormal Retinal Correspondence (page 203), "it is in this group that the greatest disappointment is encountered for only ***three*** of ***fourteen*** cases were cured by orthoptic training." However, on investigation of these fourteen cases in the table on page 199, one finds that ***three more*** of the fourteen were discharged with partial stereopsis and an angle of squint less than 3° (which as Mr. Law points out on page 194 may be regarded as

a cure), four have just started treatment, two are unable to attend, one is too young for treatment and one only is a failure.

Taking into account therefore only those cases in which treatment has been completed, we find:—

Three "cured" with full stereopsis.
Three "cured" with partial stereopsis.
One failure; *i.e.*, six "cured" out of seven.

The fact that in three out of these six cases an operation was required in addition to orthoptic treatment, should not remove them from the "cures by means of orthoptics." The four who have just started treatment obviously have a chance of being cured, and the two who are unable to attend, and the one too young must obviously not be included.

That far too much enthusiasm has been shown in certain quarters for orthoptic treatment I heartily agree, and an immense amount of time is sometimes spent in treating cases that are certainly incurable, but this fact should not be used as an argument against the value of orthoptic training. The fault sometimes lies with the ophthalmologist who insists upon referring cases to the orthoptist for treatment with a sort of half-hearted enthusiasm of "let's try exercises," when the case is clearly one that will not benefit thereby.

Ophthalmologists are familiar with the large group of accommodative squints that are "cured" with glasses alone, and it is this group of twenty-seven cases quoted by Mr. Law in which, for a cosmetic "cure," no treatment other than glasses is necessary, but one would like to know—are all these cases "straight" or "binocular" when not wearing their glasses, and if so, do they possess useful binocular visual acuity without glasses?

To quote an instance:—

A female office clerk, aged nineteen years, consulted me on account of headaches and blurring of vision when tired. She wore glasses which she had used since the age of four years for work only (+3·0 D. sph. each eye). I found her vision was 6/5 in each eye separately, but binocularly she could only read 6/36. She had three dioptres of hypermetropia and her vision with the correct glasses (which she was wearing) was 6/5 uniocularly or binocularly. She had a convergent angle of +12° with S.M.P. slides on the synoptophore without glasses, and +2° with glasses, and good fusion with stereoscopic vision.

Now it is obvious that the constant use of glasses was all that was required to effect a "cure," but she objected to wearing glasses on account of appearance, so a course of orthoptic treatment was advised as a result of which she learned to dissociate "accommodation" from "convergence," and she now reads 6/6 binocularly without glasses and finds her vision much improved. She continues with her glasses for near work.

I venture to suggest that in this class of case, orthoptic treatment is worth while, and the earlier it is administered the less likely are the symptoms to occur in later life.

I think in assessing a cure one is sometimes apt to think in terms only of performance on the synoptophore when what we really want to know is what is occurring in ordinary life.

Additional information as to the original angle of squint before wearing glasses, and the refractive error present would have been of interest in Table II.

The economic question of orthoptic treatment has been very rightly stressed by Mr. Law. In the case of children who have to travel long distances, it is often necessary to consider orthoptic treatment as unsuitable, unless the child is at the age when home-treatment supervised by an intelligent parent can be carried out.

Again in dealing with children from "uneducated homes" where their future position in life is such that the power of binocular vision is unlikely to matter very much, orthoptic treatment may be deemed superfluous.

Finally, I think it would have been more advisable to head the article "On the Value of Orthoptic Training in Cases of Concomitant Strabismus" rather than "On the Value of Orthoptic Training," since there is no doubt that in cases of heterophoria in adults, much can be done to alleviate symptoms by orthoptic measures, and a far higher percentage of successes obtained.

I would venture to suggest that the results of orthoptic treatment in the cases quoted by Mr. Law are on the whole most satisfactory.

Yours faithfully,

T. KEITH LYLE.

7, QUEEN STREET,
MAYFAIR, W.1
April 25, 1938.

NOTES

Honour

A NEW operating theatre has recently been opened at the Shrewsbury Eye, Ear and Throat Hospital while the original theatre has been enlarged. The names of Swanzy and Russ Wood have been given to these new rooms. Mr. Russ Wood worked in Shrewsbury for 31 years and it is most appropriate that the enlarged theatre should in future be known by his name. We offer him, in the name of British ophthalmology, cordial congratulations.

FUTURE ARRANGEMENTS

1938

June 10.—Section of Ophthalmology, Royal Society of Medicine (Annual Meeting).

July 7-9.—Oxford Ophthalmological Congress, at Oxford.

October 7—Midland Ophthalmological Society, at Birmingham and Midland Eye Hospital (Annual Meeting).

CONTEMPORARY OPHTHALMIC LITERATURE

Annales d'Oculistique. *April, 1938.*

ALAJOUANINE and MORAX. The tonic pupil and its relation with Adie's syndrome.
SÉDAN. Retinal haemorrhages brought on by overstrain during aviation.
GAULEJAC. Wounds attributed to aviators' glasses.

Revue Internationale du Trachome. *January, 1938.*

DELANOÉ and SÉDAN. Pyrexia and trachoma.
GRUTER. The micro-structure of the epithelial cells and their significance in the aetiology of trachoma.
SHIMKIN. Transplantation conchae auriculae as a new method of correcting spastic entropion of the upper lid following total tarsectomy.

Klinische Monatsblätter für Augenheilkunde. *March, 1938.*

MEYER. Results of treatment of lid cancer with Thorium X bacillus.
TERTSCH. Bilateral X-ray observation during operation in deciding the method of choice for the removal of a non-magnetic or weakly magnetic foreign body from the eye.
JESS. Luxation of the eyeball into the antrum of Highmore, simulation of anophthalmos on dissection.
SCHEYHING. A rare case of spontaneous orbital haemorrhage during menstruation.
JAHNKE. Experimental research on the occurrence of ectogenous iritis. Contribution to the working out of axon reflexes in the eyes.
MEYER. Benign lymphogranulomatosis (Boeck's sarcoidosis) and iridocyclitis.
CANON. Gas blisters in human eyes.
YAMAGA. Experimental researches on cysticercus fasciolaris in the anterior chamber of rabbits.
FAZAKAS. The rôle of the mould fungi in the course of eye disease.

April, 1938.

VOGT. Further ocular studies of uniovular twins; high incidence of the inheritance of senile characteristics.
ALBRICH and KUKAN. Blood pressure and intra-ocular pressure, at the same time a contribution to the pathology of tabetic optic atrophy.
SCHRECK. An oligodendro-glioma as a contribution to the primary intradural optic nerve tumours.
FAVALORO. The glial and spongioblastic origin of retinal tumours.
RICHNER. Corneal affections from a keratoma palmare et plantare hereditarium.
BLOBNER. Crystalline degeneration of the conjunctiva and cornea.

Archivos de Oftalmologia de Buenos Aires. *January, 1938.*

PEREIRA. Optico-ciliary neurotomy.
PAVIA. Congenital familial unilateral melanosis. (Benign type.)
PRADO. Thrombosis of the central retinal vein following a dental infection.
PEYRET. Pupillometry and anisocoria.
SVERDLICK. Jacobson's solution in the treatment of trachoma and of corneal opacities.